EVALUATING A CHILDHOOD DIARRHEA MANAGEMENT PROGRAM IN UTTAR PRADESH, GUJARAT AND BIHAR, INDIA: DETERMINANTS OF DIARRHEA PREVALENCE, RECALL, CARE-SEEKING AND TREATMENT

by

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A dissertation submitted to Johns Hopkins University in conformity with the requirements for the degree of Doctor of Philosophy

Baltimore, Maryland
March 2014

Abstract

Objective: The overall goal of this dissertation was to analyze factors of potential importance to evaluations of diarrhea management programs aiming to reduce the burden of diarrhea among children under-five. The specific research aims were to describe the household- and village-level determinants of diarrheal illness, care-seeking, and treatment with oral rehydration salts (ORS) (Paper 1); to determine the role of episode severity on caregiver recall, care-seeking and treatment of diarrhea (Paper 2); and to assess the association between observed prescribing practices and reported knowledge of ORS and therapeutic zinc supplementation (Paper 3).

Methods: Diarrhea management programs in Uttar Pradesh (UP), Gujarat and Bihar were evaluated using baseline and midline cross-sectional household surveys and provider assessments. Multilevel models with random effects for village and fixed effects for household- and village-level predictors were built for the log odds of diarrhea, care-seeking and ORS treatment (Paper 1). Logistic regression models with predictors for reported diarrheal symptoms were built for the log odds of distant versus recent onset, care-seeking, and ORS/zinc treatment (Paper 2). Principal components analysis was performed on public and private sector providers' responses to knowledge questions in order to generate a novel scale assessing ORS/zinc knowledge, and a binary indicator of whether ORS/zinc was prescribed during direct observation was regressed onto the resulting knowledge index scores (Paper 3).

Results: Multilevel models for all outcomes showed evidence of statistically significant inter-village variation, and fixed effects were observed for both household- and village-level predictors (Paper 1). Symptoms suggestive of increased episode severity were associated with distant versus recent onset, care-seeking, and ORS/zinc treatment (Paper 2). As measured by a novel scale, ORS/zinc knowledge was associated with higher odds of ORS/zinc prescribing among public and private sector providers (Paper 3).

Conclusions: Evaluations of diarrhea management programs should consider inter-village variation and both household- and village-level predictors in the estimation of prevalence and coverage. Cross-sectional surveys should collect data with one-week recall to avoid missing information on episode occurrence and care-seeking/treatment practices. Programmatic activities should center on increasing knowledge of ORS and zinc among public and private sector providers through biannual trainings but should also focus on ensuring sustained access to an adequate supply chain.

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Acknowledgements

This dissertation would not have been possible without the contributions of many individuals. I would like to thank my advisor, Dr. Robert E. Black, for his invaluable guidance and expertise. I am also extremely grateful to Dr. Christa Fischer Walker for her incredible support and mentorship over the past five years. I have learned a great deal from both of them, and my research has benefited from their technical knowledge.

I would like to acknowledge the researchers at the Society for Applied Studies (SAS) in New Delhi. I was fortunate to have worked with Dr. Sunita Taneja, Dr. Sarmila Mazumder, and Dr. Nita Bhandari while in India. I also owe a special thank you to the hardworking members of the data collection team that helped me navigate rural Bihar; I was sincerely impressed by their dedication and will never forget that they climbed hills and crossed rivers in order to reach the providers that had been randomly selected so easily from an office in Baltimore.

I am greatly appreciative to all of the professors and faculty that have assisted me during my time at Johns Hopkins. In particular, I would like to thank the members of my preliminary and final oral examination committees: Dr. Kenrad Nelson, Dr. Cynthia Minkovitz, Dr. Deanna Kerrigan, Dr. Lawrence Moulton, Dr. Mathuram Santosham, Dr. Joanne Katz, and Dr. Abdullah Baqui. I would also like to express gratitude to my fellow PhD students for helping me to feel part of a supportive, collaborative community.

Finally, I am indebted to the family and friends that have supported me during this venture and throughout my life. I am especially grateful to my mother, Renee, who was my first and most important teacher and to my husband, Francesco, for his endless reassurance and encouragement.

Support

Tuition support for this degree program was provided by the Johns Hopkins School of Public Health Department of International Health. The Office of the National Coordinator/ Academic Recovery and Reinvestment Act's Informatics Workforce Training grant provided additional tuition support in academic year 2012-2013.

Project funding and salary support were made available through the following grants awarded to the Bill and Melinda Gates Foundation via US Fund for UNICEF and the Children's Investment Fund Foundation, respectively: "Enhancing the uptake of ORS and zinc in targeted areas of India" and "Reducing deaths from diarrhea in the Indian state of Bihar."

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List of Abbreviations and Acronyms

ASHA	Accredited Social Health Activist
AWW	Anganwadi worker
ANM	Auxiliary Nurse Midwife
AYUSH	Ayurveda, Unani, Siddha, Homeopathy
BMGF	Bill and Melinda Gates Foundation
CIFF	Children's Investment Fund Foundation
DAZT	Diarrhea Alleviation through Zinc and ORS Treatment program
GAPPD	Global Action Plan for Pneumonia and Diarrhea
IAP	Indian Academy of Pediatrics
IMA	Indian Medical Association
IMCI	Integrated Management of Childhood Illnesses
JHU IIP	Johns Hopkins University Institute for International Programs
MO	Medical Officer
MI	Micronutrient Initiative
MDG4	Millennium Development Goal 4
NFHS	National Family Health Survey
NRHM	National Rural Health Mission
ORS	Oral rehydration salts
ORT	Oral rehydration therapy
PHC	Primary Health Center
PCA	Principal components analysis
PPS	Probability proportional to size sampling
RHF	Recommended home fluids
RMP	Rural medical practitioner
SAS	Society for Applied Studies
SES	Socioeconomic status
UNICEF	United Nations Children's Fund
UP	Uttar Pradesh
WHO	World Health Organization

Chapter One: Background

1.1. Introduction

Diarrhea is a leading cause of morbidity and mortality among children under-five worldwide [1, 2]. In 2013, the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) published the integrated Global Action Plan for Pneumonia and Diarrhea (GAPPD), which outlined a framework for ending preventable child deaths due to diarrhea and pneumonia by 2025 [3]. The GAPPD aims to decrease diarrhea-attributable mortality to <1 death per 1000 live births and to reduce the incidence of severe diarrhea by 75% compared to 2010 levels by 2025 [3]. In order to attain these targets, coverage of appropriate diarrhea management must increase to 90% by 2025, and access to sanitation and drinking water should be universal in healthcare facilities and households by 2030 [3].

The GAPPD emphasizes a "protect, prevent, treat" approach that integrates interventions of proven effectiveness, such as exclusive breastfeeding for the first 6 months of life, complementary feeding, vitamin A supplementation, sanitation and hand washing with soap, improved care-seeking, continued feeding, and treatment with oral rehydration salts (ORS) and zinc [3]. Though scale-up of these interventions does not require additional technology, countries may encounter challenges implementing diarrhea management programs across diverse communities, motivating mothers to seek care for symptoms of perceivably low severity, and changing provider behavior with regard to prescribing practices.

Using data from the large-scale evaluation of a diarrhea management program in three states in India, this dissertation analyzed various factors of potential importance to countries during scale-up of ORS, zinc and other childhood diarrheal control interventions. Paper 1 investigated the household- and village-level influences of diarrheal illness, care-seeking and ORS treatment for diarrhea in young children, and Paper 2 assessed the extent to which episode severity affects the care-seeking and ORS/zinc treatment practices of caregivers of children under-five. Paper 3 evaluated the association between provider knowledge and observed ORS/zinc prescribing behavior among public sector and informal private sector health workers. The results of these three studies may inform programmatic activities and evaluations centered on reducing the burden of diarrhea among children under-five in India.

1.2. Literature Review

1.2.1. The burden of diarrhea among children under-five globally

Though the annual number of global deaths among children under five years of age has dropped from 12.4 million in 1990 to 7.6 million in 2010 and 6.9 million in 2012 [1, 4], high child mortality rates of >100 under-five deaths per 1000 live births persist in 24 countries and threaten progress towards Millennium Development Goal 4 (MDG4), which aims to reduce the global under-five mortality rate, between 1990 and 2015, by two-thirds [5]. Lagging progress towards MDG4 is due in part to failed scale-up of effective interventions and treatments for diarrhea, the third leading killer of children under-five globally, after pneumonia and neonatal deaths [1].

The global burden of diarrhea among children under-five was first summarized by a meta-analysis published in 1982, which estimated the 1954-1979 median incidence of diarrhea as 2.2 -3.0 episodes per child per year. Given population levels at the time, this translated into an annual occurrence of between 744 million and 1 billion diarrheal episodes and 4.6 million diarrhea-associated deaths among children under-five globally [6]. In 1990, an updated meta-analysis of studies published between 1980 and 1990 reported no change in diarrhea incidence (2.6 episodes per child per year) but a substantial decrease in annual mortality (3.3 million deaths per year) [7]. Pooled estimates published in 2003 indicated another decline in diarrhea-associated mortality (2.5 million deaths per year) but no change in median incidence (3.2 episodes per child per year) [8]. By 2011, global diarrheal disease mortality among children under-five had dropped to 711,800 deaths per year, but global incidence remained relatively stagnant at 2.9 episodes per child under-five per year [9]. Despite decreases in diarrheal deaths over time, coverage of protective, preventive and therapeutic interventions must be further improved in order to accelerate global progress towards ending diarrhea as a preventable cause of death among young children [3].

1.2.2. The definition and clinical manifestations of diarrhea

Diarrhea is defined as the passage of at least three liquid/ loose /watery stools within a 24-hour period. Diarrheal episodes are typically defined as a period of diarrhea separated by an interval of two to three diarrhea-free days. The WHO identifies three clinical types of diarrhea: acute watery, acute bloody (also called dysentery) and persistent [10]. Acute episodes last several hours or days; whereas, persistent episodes last ≥ 14 days. According to a meta-analysis of 41 studies on children under-five, the average duration of diarrheal episodes is 4.3 days (95% CI: 4.2-4.4 d) among community cases and 8.4 days (95% CI: 8.1-8.8 d) among hospital inpatients [11].

Diarrhea leads to rapid loss of water and electrolytes and subsequent dehydration if liquids are not replaced with ORS. Early dehydration does not exhibit signs or symptoms; moderate dehydration involves thirst, restlessness, decreased skin elasticity and sunken eyes; severe dehydration results in the symptoms of moderate dehydration plus those of increased severity, including shock, altered consciousness, pale skin and low blood pressure [10]. Without ORS or IV drip treatment and continued feeding, severe dehydration can lead to death [10]. Among children under-five in developing countries, diarrhea has a case fatality rate of 0.2% (95% CI: 0.1-0.5%) [12]. In clinical settings, the severity of diarrheal episodes is often described in terms of a scale, such as the Vesikari scoring system, intended to summarize the gravity of an episode with regard to dehydration signs and symptoms, duration, stool frequency, and the presence of fever, vomiting or blood in stools [13].

1.2.3. *Diarrhea etiology, transmission and risk factors*

Infectious diarrhea can result from a range of pathogens, including viruses, bacteria and protozoa. Among children worldwide, rotavirus is the leading cause of severe acute diarrhea, accounting for a median of 38.2% of diarrhea-associated hospital admissions [14]. Other common enteropathogenic causes of under-five gastrointestinal infections include *Shigella*, *Vibrio cholerae*, enterotoxigenic *Escherichia coli* (ETEC), cryptosporidium, campylobacter and salmonella [14]. Diarrheal pathogens are mostly transmitted via the fecal-oral route through ingestion of contaminated food or water. As such, inadequate personal hygiene, poor sanitation, limited access to clean water, and unsafe disposal of human feces are key risk factors for contracting such pathogens.

Reductions in the risk of diarrhea associated with hand washing with soap, improved quality of drinking water, and safe disposal of human feces have been estimated at 48%, 17% and 36%, respectively [15]. Additional risk factors for diarrhea include those associated with development, such as poor socioeconomic status, crowding, and low maternal education [12].

Nutritional determinants are also important risk factors for diarrhea infection. There is a cyclical relationship between diarrhea and malnutrition such that children with repeat diarrheal infections are at higher risk of malnutrition and stunting, and malnourished children are at elevated risk for diarrhea-associated death [2]. Moreover, the failure to exclusively breastfeed infants during the first 6 months of life and to partially breastfeed in the 18 months thereafter, also increases the risk of diarrheal morbidity and mortality [16]. Preventive routine, preventive short course and therapeutic supplementation with zinc reduce diarrhea incidence, prevalence and severity—effects which are intensified among zinc deficient children [17]. Similarly, vitamin A supplementation reduces diarrheal severity and deaths due to diarrhea as a secondary infection after measles [18, 19].

Immunizations protect against diarrhea-associated mortality by (1) reducing the risk of infection with certain enteropathogens and by (2) preventing illnesses of which diarrhea is a complication [19]. Examples of the former include the rotavirus vaccine, which is highly efficacious (80-90%) and globally recommended [20], and the cholera vaccine, which is recommended for use in cholera-endemic regions [21]. As diarrhea is a major complication of measles infection, the measles vaccine also reduces diarrheal morbidity and mortality; it has been estimated that high global coverage of measles vaccination could reduce diarrheal mortality by 6-26% among children under-five [22].

1.2.4. Geographic distribution of diarrheal morbidity and mortality among children under-five

The incidence of diarrhea among children under-five varies geographically. In 2010, the global number of episodes per child-year was 2.9, and region-specific rates ranged from 4.0 in Europe and the Americas, to 3.3 in Africa, 3.0 in the Eastern Mediterranean, 2.4 in South East Asia and 2.3 in the Western Pacific [9]. The global distribution of under-five diarrheal mortality is more heavily skewed; in 2010, the majority of deaths occurred in the WHO regions of Africa (51.6%) and South East Asia (28.0%), compared to the Eastern Mediterranean (15.4%), Western Pacific (2.8%), Americas (1.4%) and Europe (0.8%) [1]. Furthermore, only five countries (India, Nigeria, Democratic Republic of Congo, Pakistan, and Ethiopia) accounted for the bulk of under-five diarrheal deaths [1].

1.2.5. The burden of diarrhea among children under-five in India

Approximately one-fourth of global diarrheal deaths among children under-five occur in India [1]. In 2010, 0.212 million of the 1.682 million deaths (12.6%) that occurred among children under-five in India were attributable to diarrhea [1]. During that same period, the respective age-specific diarrheal incidence rates were 2.50, 3.82, 3.09 and 1.98 episodes/child-year among Indian children 0-5, 6-11, 12-23 and 24-59 months of age [9]. Discrepancies in wealth and development across India have led to differentials in diarrheal proportionate mortality across the West (9%), South (11%), North (13%), East/Central (15%) and Northeast (16%) regions [23]. In addition, gender bias has been documented with higher diarrhea-specific mortality rates occurring among girls compared to boys under five years of age [23].

1.2.6. Prevention and treatment of diarrhea among children under-five

As discussed in section 1.1, UNICEF and WHO issued the Integrated Global Action Plan for Pneumonia and Diarrhea (GAPPD) in 2013 [3]. The report outlined strategies to help countries reduce diarrheal mortality by 2025, advocating for the promotion of rotavirus and measles vaccination; vitamin A supplementation; early, exclusive breastfeeding; hand washing with soap; improved drinking water quantity and quality; community-wide sanitation; reduced osmolarity ORS for the prevention and treatment of dehydration, and zinc supplementation for 10-14 days following diarrhea onset [3].

1.2.7. Oral rehydration salts (ORS)

Until the late 1960s, the only available method for treating dehydration, the main complication of diarrhea, was to administer intravenous (IV) fluids [24]. During a diarrheal episode, prompt treatment of dehydration, which is defined as the loss of water and dissolved salts/electrolytes from the body, is essential to child survival since dehydration is the immediate cause of death in most cases of diarrhea-associated mortality [25]. Treatment of dehydration with IV fluids, however, was not logistically feasible in resource-poor settings due to high cost and the need for trained personnel to administer fluids intravenously [26].

The 1960s discovery of sodium and glucose co-transport in the small intestine was an important breakthrough that led to the invention of ORS—a lifesaving treatment for diarrhea that operates on the foundation that the absorption of water and solute (i.e. sodium ions) is accelerated in the presence of glucose [27, 28]. Early formulations of ORS contained varying concentrations of glucose and electrolyte salts dissolved in water [25].

The earliest clinical trials of ORS were conducted in Dhaka, Bangladesh and Kolkata, India in the late 1960s and demonstrated that ORS was effective in treating and preventing fluid loss compared to IV therapy [29-31]; true randomized controlled trials (RCTs) assessing the efficacy of ORS do not exist since IV therapy was considered standard of care at the time, making randomization to placebo unethical [26]. Additional studies conducted in South Asia during the 1960-70s confirmed the ability of ORS to both maintain fluid levels and rehydrate individuals with diarrhea resulting from any etiologic cause [32-34]. In response to this growing body of evidence, WHO issued a formal recommendation for the use of an ORS formulation with 90 mmol/L of sodium, 111 mmol/L of glucose and a total osmolarity of 311 mmol/L to both prevent and treat dehydration [24, 25]. This formulation was considered standard for over two decades and was extremely influential in reducing the number of global diarrhea-associated under-five deaths from 4.6 million in 1980 to 3.3 million in 1990 and to 1.5 million one decade later [6, 35].

Despite the apparent success of ORS, researchers continued to investigate improved formulations that could potentially decrease stool output and lessen the likelihood of adverse effects, such as hypertonicity (i.e. higher osmotic pressure) on net fluid absorption [25]. Emerging studies during the late 1980s and 1990s suggested that decreasing the concentration of sodium and glucose could further enhance water absorption and decrease stool volume [36]. In a meta-analysis of RCTs comparing the efficacy of reduced osmolarity solution (with a total osmolarity of 245 mmol/L) to the standard ORS formulation, it was found that the former reduced the need for supplemental IV fluids by 33%, stool output by 20%, and vomiting by 30% [24, 25]. In 2004, UNICEF and WHO issued a joint recommendation for the prompt use of reduced osmolarity ORS to treat diarrheal episodes of all etiologies among children under-five years of age [37]. The composition of reduced osmolarity ORS includes glucose, which induces the absorption of sodium (and thus water); potassium and sodium to replenish ions lost through loose stools and vomiting; and citrate to ameliorate the acidosis that results from dehydration (Table 1.1) [25].

The advent of a simple solution that could be prepared and administered by unskilled caregivers revolutionized diarrhea management by diminishing the need for hospital referrals and expensive intravenous treatment [29]. Still, national diarrhea management programs have encountered barriers to mass producing and distributing ORS at scale since the initial WHO recommendation. To supplement low ORS coverage in the 1980s, programs began to promote the use of recommended home fluids (RHFs) as an approach to prevent dehydration, whereby RHFs comprised homemade mixtures of sodium and glucose, rice water solutions, cereal-based solutions, soups, juices and teas [35]; however the effectiveness of RHFs was not established.

In 1988, oral rehydration therapy (ORT), which was previously synonymous with ORS, was redefined as the process by which fluid is administered orally to prevent or treat diarrhea-associated dehydration, thereby encompassing both ORS and RHFs [35]. The resulting category confused the interpretation of coverage indicators and did not clearly delineate the individual benefits of ORS and RHFs [26, 35]. A meta-analysis aiming to separate the effects of ORS and RHFs was published in 2010 [26]; this review estimated a 69% (95% CI: 51-80%) reduction in diarrhea-associated mortality among communities with ORS promotion versus comparison communities but uncovered insufficient data to estimate the effect of RHFs on mortality.

1.2.8. Therapeutic zinc supplementation

Diarrhea is associated with poor nutrient absorption, which results from rapid transit in the gut and the breakdown of absorptive mucosa [38]. Specifically, there is a link between diarrheal illness and both the malabsorption and loss of endogenous zinc, as established by studies published during the 1970s and 1980s [39-41]. Zinc is an essential micronutrient that plays an important role in cellular metabolism [41]. There is therefore an interaction between the deficits in zinc that result from a diarrheal episode and the impairments in cellular immunity that make an individual more susceptible to repeated infection with diarrheal pathogens and subsequent zinc deficiency and malnutrition [38, 42]. As illustrated by Figure 1.1 [38], zinc deficient and malnourished children are increasingly susceptible to transmission of diarrheal pathogens, thus promulgating the vicious cycle between nutritional deficiency and infection [42].

The earliest RCT assessing the efficacy of zinc as a potential treatment for diarrhea infection was published by Sachdev et al. in 1988 [43, 44]. The study was conducted in India in a population of 50 6-18 month-old children hospitalized for acute diarrhea of which half were randomized to placebo and the other half to daily supplementation with 40 mg of elemental zinc. The results showed that zinc supplementation decreased the duration of diarrheal episodes by 9% and stool frequency by 18% as compared to placebo. Furthermore, children with lower levels of rectal mucosal zinc experienced greater reductions in duration and stool frequency. Although none of these findings were statistically significant, they signified important implications for the potential impact of therapeutic zinc on child survival.

The evidence base supporting zinc as an efficacious treatment for acute infectious diarrhea was bolstered by a number of RCTs conducted during the late 1980s and 1990s [44-46]. Studies reporting reductions in the stool frequency and duration of acute diarrhea among zinc-treated children included a hospital-based trial in Bangladesh [47], and community-based trials in Indonesia [48], India [49], and Bangladesh [50]. Additionally, zinc-treated patients enrolled in the hospital-based RCT benefited from reduced stool output [47]. Pooled data from the three community-based studies indicated that episodes lasting longer than seven days occurred 25-43% less frequently among children receiving zinc compared to placebo [44, 47-49].

Several studies also reported modification by nutritional status of the effect of zinc treatment on acute diarrhea. Among acute-diarrheic children randomized to zinc, greater reductions in duration and severity were observed in stunted children in the community [49], and in hospitalized children with low plasma zinc concentration (<14 μmol/L) [47]. Furthermore, the reductions in diarrheal morbidity and frequency were markedly greater among stunted compared to non-stunted children in the zinc arm of an RCT in Ethiopia [51].

In addition to acute diarrhea, early studies also supported the efficacy of zinc in the treatment of persistent diarrhea. The first efficacy trial of children with persistent diarrhea was conducted by Sachdev et al. on a sample of 40 hospitalized children 6-18 months of age and reported a 19%, albeit not statistically significant, reduction in duration among zinc-treated children [44, 52]. This trend was confirmed by additional hospital-based RCTs in Bangladesh and Pakistan, which also suggested a stronger effect among undernourished children and those with lower levels of plasma zinc [47, 53]. A community-based trial of children 6-36 months of age in Peru provided further support for these findings [54].

In order to summarize the growing body of evidence for a therapeutic effect of zinc on acute and persistent diarrhea, the Zinc Investigators' Collaborative Group published a meta-analysis in 2000 [55]. The meta-analysis included outcomes reported by three RCTs on acute diarrhea and four RCTs on persistent diarrhea. The pooled results showed that among zinc-treated children under-five, mean duration was 16% (95% CI: 7-26%) shorter for acute episodes and 29% shorter for persistent (95% CI: 6-53%) episodes (Table 1.2). Furthermore, among zinc-treated children, the probability of continued diarrhea was reduced by 15% (95% CI: 8-22%) for acute episodes and by 24% (95% CI:

8-38%) for persistent episodes. Children randomized to zinc experienced a 27% (95% CI: 2-45%) lower rate of prolonged episodes compared to placebo.

From 2000-2010, subsequent RCTs assessing the consistency of earlier trials confirmed that the efficacy of therapeutic zinc could be generalized to various populations and settings [56-63]. A Cochrane review published in 2008 and a meta-analysis published in 2009 corroborated previously published findings on the efficacy of zinc in reducing diarrhea-associated morbidity among children under five years of age [64, 65]. The meta-analysis reported a pooled reduction of 0.5 days for the duration of acute episodes and 0.68 days for the duration of persistent episodes ($p<0.05$) (Table 1.2) [65]. In response to the mounting body of evidence, UNICEF and WHO issued a joint global recommendation in 2004. In addition to reduced osmolarity ORS, the revised guidelines advised daily supplementation with 20 mg of zinc for children ≥ 6 months and with 10 mg of zinc for children <6 months of age for 10-14 days immediately following diarrhea onset [37].

During the same period, cluster-randomized trials in Bangladesh and India sought to establish the effectiveness of therapeutic zinc intervention [66, 67]. In a cluster randomized trial of 8000 children in Bangladesh, Baqui et al. reported a 15% (95% CI: 4-24%) reduction in diarrhea incidence and a 24% (95% CI: 10-35%) decrease in episode duration among children living clusters where therapeutic zinc intervention was made available [66]. In a cluster randomized trial of 20,000 caregivers in India, Bhandari et al. observed 25% (95% CI: 9-38%) and 44% (95%CI: 25-59%) reductions in 24-hour and two-week diarrhea prevalence, respectively, and a 59% (95% CI: 43-71%) reduction in all-cause hospitalization in therapeutic zinc intervention clusters [67].

The evidence supporting the efficacy of zinc for the treatment of acute and persistent diarrheal episodes has primarily been consistent, yet there has also been evidence suggesting that an effect among infants <6 months of age is lacking. RCTs in Bangladesh, Ethiopia, Pakistan, and India reported no difference in the duration and severity of acute episodes among zinc-treated infants 1-5 months of age compared to those randomized to placebo [68, 69]. On the contrary, the results of two cluster-randomized trials conducted in Bangladesh and India reported shorter duration and decreased incidence among zinc-treated infants <6 months of age, mirroring trends observed in older children [70, 71].

Therapeutic zinc has also been demonstrated to be efficacious in reducing diarrhea-associated hospital admissions and mortality among children under-five [66, 67]. A meta-analysis of two cluster-randomized trials showed a 23% (95% CI: 15-31%) decrease in hospital admissions for diarrhea in zinc treatment intervention clusters compared to control clusters (Table 1.2) [72]. In a cluster-randomized trial in 2002, Baqui et al. reported a 51% (95% CI: 6-75%) reduction in the rate of non-injury related deaths among communities receiving zinc intervention [66]; this remains the only trial with adequate power to detect a mortality effect [72].

1.2.9. ORS and zinc coverage and treatment policies

Figures 1.2 and 1.3 illustrate the countries that had incorporated reduced osmolarity ORS and therapeutic zinc supplementation into their diarrhea control policies as of 2011. Figure 1.4 depicts the delivery channels through which recommended diarrhea treatment is available, globally. Despite growth in the number of national policies supporting reduced osmolarity ORS and therapeutic zinc, coverage remains low. The coverage of ORS in developing countries was approximately 35% in 2012 [3], which was not much improved compared to the 2000 (28%) and 2010 (34%) estimates [19, 73]. Similarly, coverage of ORT (i.e. ORS or RHFs or increased fluids) with continued feeding was only 39% in developing countries in 2010 [73]. Global estimates of zinc coverage are largely unavailable but are expected to be lower than ORS coverage.

An additional goal of national programs is to decrease the irrational use of antibiotics. Enhanced uptake of zinc has been linked to reductions in the misuse of antibiotics and increases in the use of ORS to treat diarrhea [74]. Efforts to scale up zinc are therefore of great importance.

1.2.10. ORS and zinc treatment policies, practices, and challenges in India

In 2003 and again in 2006, the Government of India (GoI) and the Indian Academy of Pediatrics (IAP) issued revised guidelines for the management of diarrhea in India. The new recommendations included reduced osmolarity ORS for the treatment of all diarrhea types across all age groups and daily zinc supplementation for 14 days with 20 mg zinc in children 7-59 months of age and 10 mg in children 2-6 months of age [75, 76]. Despite the existence of these guidelines, ORS and zinc coverage rates remain low. According to the National Family Health Survey (NFHS-3), only 33% and 0.3% of children under five suffering from diarrhea in the two-weeks prior to the survey received ORS and therapeutic zinc, respectively [77].

In India, both low osmolarity ORS and zinc products are available through the public and private sectors [78]. At present, zinc is manufactured by at least 16 companies in India, and ORS is also locally produced [78]. Although the country's production capacity is sufficient to meet its needs, zinc is not widely available through either sector; ORS is more widely available but also suffers from interruptions in availability [79].

The Indian Diarrheal Disease Control Program is focused on scaling up access and promoting the early and proper use of ORS and zinc [80]. Although prevention is also a fundamental goal of the program, the success of preventive interventions is hindered by conditions in urban slums and rural areas, such as overcrowding, inadequate sanitation, contaminated drinking sources, poor hand and food hygiene and open defecation [19, 80]. In the absence of adequate control over environmental risk factors, rapid scale-up of ORS and zinc is pivotal to curbing diarrheal deaths among Indian children.

India has a complex health system with a diverse range of stakeholders working in the public and private sectors. The national program is dedicated to improving and increasing the availability of diarrhea treatment through primary health care workers operating within the government sector [80]. The public health sector consists of several levels in each district: the district hospital, the community health centers (CHC), the primary health center (PHC) and the sub-health center (SHC). District hospitals, CHCs and SHCs are positioned to cover populations of 2-3 million, 100,000-300,000, and ~5,000, respectively [81]. The population covered by PHCs varies by state; for example, PHCs cater to a population of 30,000 in Gujarat and 150,000 in UP. Providers stationed at the PHC, such as medical officers (MOs) and auxiliary nurse midwives (ANMs), are essential to the treatment of under-five diarrhea cases. However, ANMs and accredited social health activists (ASHAs) that transition between the PHC and the village have the ability to interact with villagers and are therefore ideally positioned to both detect and treat diarrhea cases at the community-level. Anganwadi workers (AWW) are an additional cadre at the community-level that is generally responsible for pre-school education but is also tasked with health mobilization activities. AWWs do not typically carry or dispense medication, but several state governments have issued or are considering provisions allowing AWWs to distribute both ORS and zinc.

Despite efforts to promote the utilization of public sector services for diarrhea treatment, as much as 80% of diarrhea care-seeking takes place through the private sector [77, 82]. While formal private sector practitioners and institutions are well-established in India, the private sector is mostly comprised of informal providers, referred to as rural medical practitioners (RMPs). The term RMP encompasses most individuals providing health services outside the government sector. The population of RMPs consists of providers with formal government-recognized degrees in modern allopathic and traditional *'Ayush'* (Ayurveda, Unani, Siddha, Homeopathy) medicine, as well as those with unrecognized degrees, informal training or no training at all [82-84]. Studies conducted in UP, West Bengal and Karnataka have reported that the majority of RMPs belong to the latter group of unregistered, untrained providers [82-84]. In spite of the largely unqualified and unregulated nature of RMP services, RMPs provide accessible and low-cost options for care in, mostly rural, areas where no treatment is the only alternative [82, 84]. As such, RMPs play an important role in diarrhea treatment; diarrhea is among the most common RMP-treated illnesses, and typically RMP-prescribed regimens do not include ORS and zinc but rather injections, antibiotics and anti-diarrheals [82-84].

1.3. Objectives and Rationale

1.3.1. Overall goal and specific aims

The overall goal of this dissertation was to analyze factors of potential importance to evaluations of childhood diarrhea management programs. In working towards this objective, focus was placed on identifying and increasing understanding of the determinants affecting prevalence, recall, care-seeking and treatment of diarrhea among children under-five in Uttar Pradesh, Gujarat and Bihar, India. The following specific aims were addressed:

- Specific Aim 1: To describe the household- and village-level determinants of diarrheal illness, care-seeking, and ORS treatment among children 2-59 months of age in Uttar Pradesh and Gujarat, India.
- Specific Aim 2: To determine the role of episode severity on caregiver recall, care-seeking and treatment of diarrhea among children 2-59 months of age in Uttar Pradesh, Gujarat and Bihar, India.
- Specific Aim 3: To assess the association between observed prescribing practices and reported knowledge of ORS and zinc treatment for childhood diarrhea among public- and private-sector providers in Uttar Pradesh, Gujarat and Bihar, India.

1.3.2 Rationale for specific aim 1

Diarrhea management programs can benefit from research on the relative importance of the factors influencing key program outcomes, such as diarrhea prevalence and coverage of care-seeking and ORS. There is evidence suggesting that these outcomes may be affected not only by attributes of the individual and household, but also by traits of the community [85-88]. Studies in Sub-Saharan Africa and Brazil have concluded that diarrhea duration and the decision to seek care outside the home are influenced by both household wealth and the degree of socioeconomic development in the surrounding community [85, 86]. In addition, community-level measures of improved sanitation have been shown to reduce the risk of diarrhea among children under-five, even after controlling for household-level hygiene, food preparation and toilet/latrine access [86, 88]. Collective measures of maternal knowledge may also impact outcomes important to improving diarrhea management programs; a study in Burundi reported an effect of community-level social-support on ORS usage among women from both rural and urban regions [87].

Further research is warranted to assess the extent to which determinants at the household- and village-level impact care-seeking and treatment for diarrhea in young children within the context of rural India. The results of such research would shed light on the need for programs and program evaluations to focus on factors beyond household demographics and practices.

1.3.3 Rationale for specific aim 2

Studies have suggested that measures of two-week diarrhea prevalence underestimate the true burden of illness in populations of children under-five due to waning recall among caregivers over time [89-91]. In addition, recall is reportedly more accurate among caregivers of children that exhibited severe symptoms [89-93]. Though studies assessing the two-week prevalence of diarrhea routinely collect data on the characteristics and symptoms of recalled episodes, definitions for what constitutes severe have varied. In Bangladesh and Guatemala, less biased recall has been linked to symptoms of increased severity, such as higher stool frequency, vomiting, and the presence of blood in stools [89, 90].

There is also evidence that caregivers' perceptions concerning episode severity and the relative importance of various symptoms in young children influence the decision to seek care and treatment outside the home [94, 95]. In Kolkata, India, care was more frequently sought for children in which diarrhea was accompanied by lethargy, sunken eyes and dry mouth [94]. Longer duration of illness has also been shown to increase utilization of health care facilities [95].

The potential effect of episode severity on recall, care-seeking and treatment may have important implications for evaluations of diarrhea management programs, which aim to accurately measure program outcomes and impact. Research is necessary to establish whether reported symptoms of diarrhea influence estimates of prevalence, care-seeking and ORS/zinc treatment among children under-five in rural India.

1.3.4 Rationale for specific aim 3

In India, efforts to scale-up ORS and zinc supplementation for the treatment of childhood diarrhea require the participation of AWWs, ASHAs, and RMPs in order to be successful. As such, diarrhea management programs allocate resources to training such providers in adequate treatment practices. Many evaluations are designed to assess the knowledge of trained providers as a key program output, but the association between knowledge and practice is often not considered. Increases in provider knowledge alone are not sufficient to achieve program outcomes and impact if knowledge does not translate into improved practice. Studies in the Gambia and Vietnam have demonstrated that high levels of knowledge about diarrhea and ORS are not necessarily correlated with correct prescribing [96, 97].

Diarrhea management programs and program evaluations in rural India would benefit from research on the association between observed prescribing practices and reported knowledge of ORS and zinc among RMPs, ASHAs and AWWs. Such research would highlight the relative importance of investing programmatic resources and inputs on the training of RMPs, ASHAs and AWWs.

Table 1.1

Composition of reduced osmolarity ORS

	grams/liter	%		mmol/liter
Sodium chloride	2.6	12.683	Sodium	75
Glucose, anhydrous	13.5	65.854	Chloride	65
Potassium chloride	1.5	7.317	Glucose, anhydrous	75
Trisodium citrate, dehydrate	2.9	14.146	Potassium	20
			Citrate	10
Total	**20.5**	**100**	**Total Osmolarity**	**245**

Source: WHO/UNICEF: Oral Rehydration Salts: Production of the New ORS. 2006[25].

Table 1.2

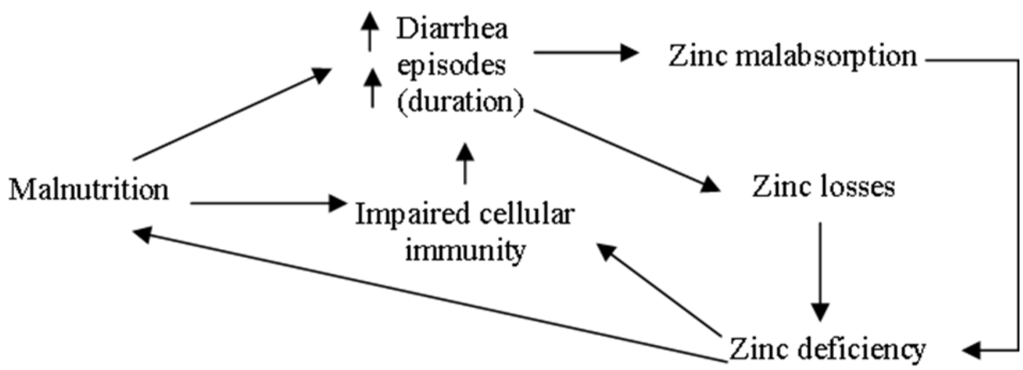
Summary of the effect of therapeutic zinc on diarrheal morbidity outcomes

Outcome Measure	**Effect Size (95% CI)**	**Number of Studies Year of Publication [Ref]**
Mean Duration of Acute Episodes	16% reduction (7-26%)	3 2000 [55]
	reduction by 0.5 d (0.18-0.82)	14 2009 [65]
Mean Duration of Persistent Episodes	27% reduction (2-45%)	4 2000 [55]
	reduction by 0.68 d (-0.01-0.64)	5 2009 [65]
Diarrhea Hospitalizations	23% reduction (15-31%)	2 2010 [72]

Source: Fischer-Walker C, Lamberti L, Roth D, Black R: Zinc and infectious diseases. In: Zinc in Human Health. edn. Edited by Rink L. Amsterdam: IOS Press; 2011: 234-253 [17].

Figure 1.1

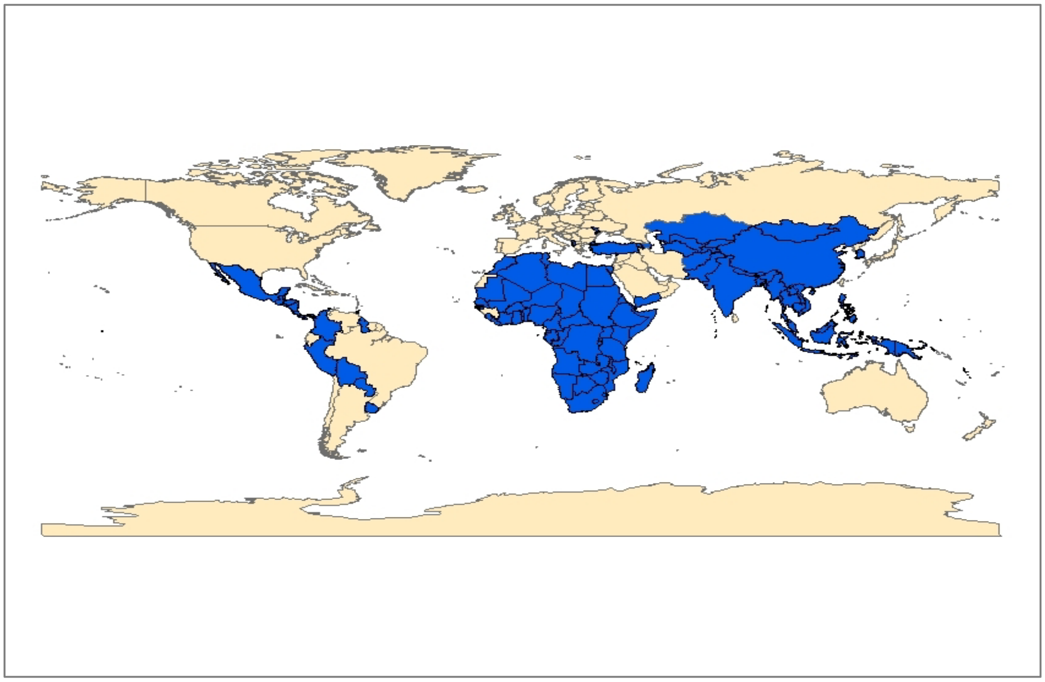
Schematic of the interaction between diarrhea, zinc deficiency, and malnutrition



Recreated from source: Wapnir RA: Zinc deficiency, malnutrition and the gastrointestinal tract. J Nutr 2000, 130(5S Suppl):1388S-1392S [38].

Figure 1.2

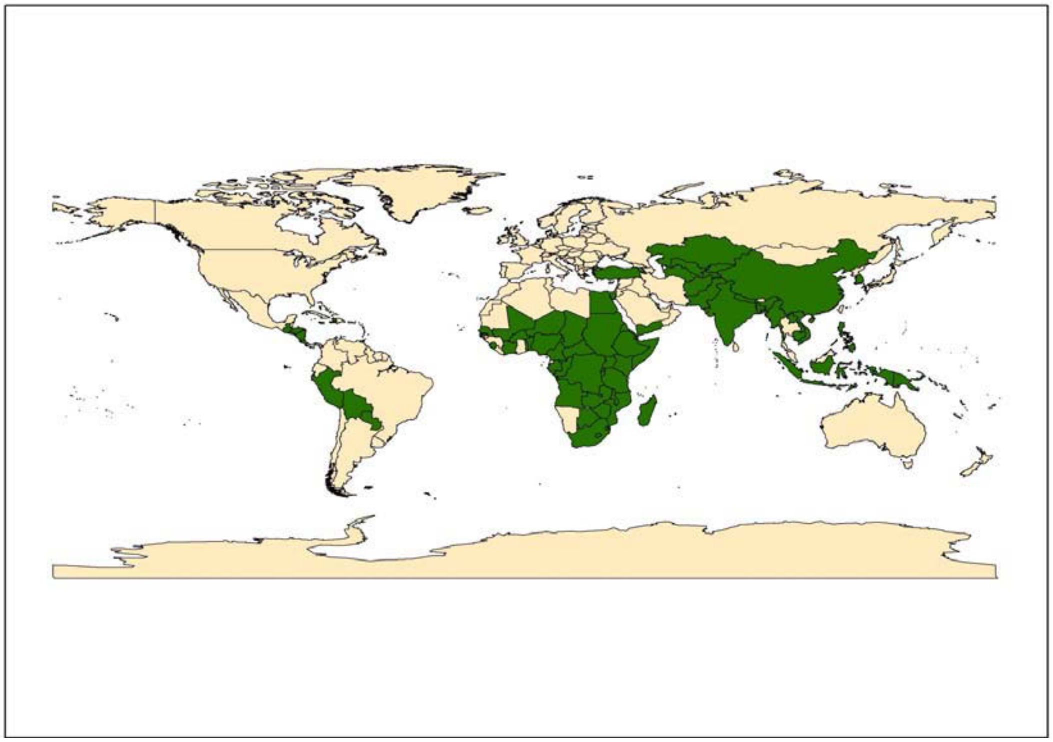
Countries with diarrhea management policies that include reduced osmolarity ORS, 2011



Source: Zinc Task Force; Personal correspondence with Christa Fischer-Walker, PhD, JHSPH, 2011.

Figure 1.3

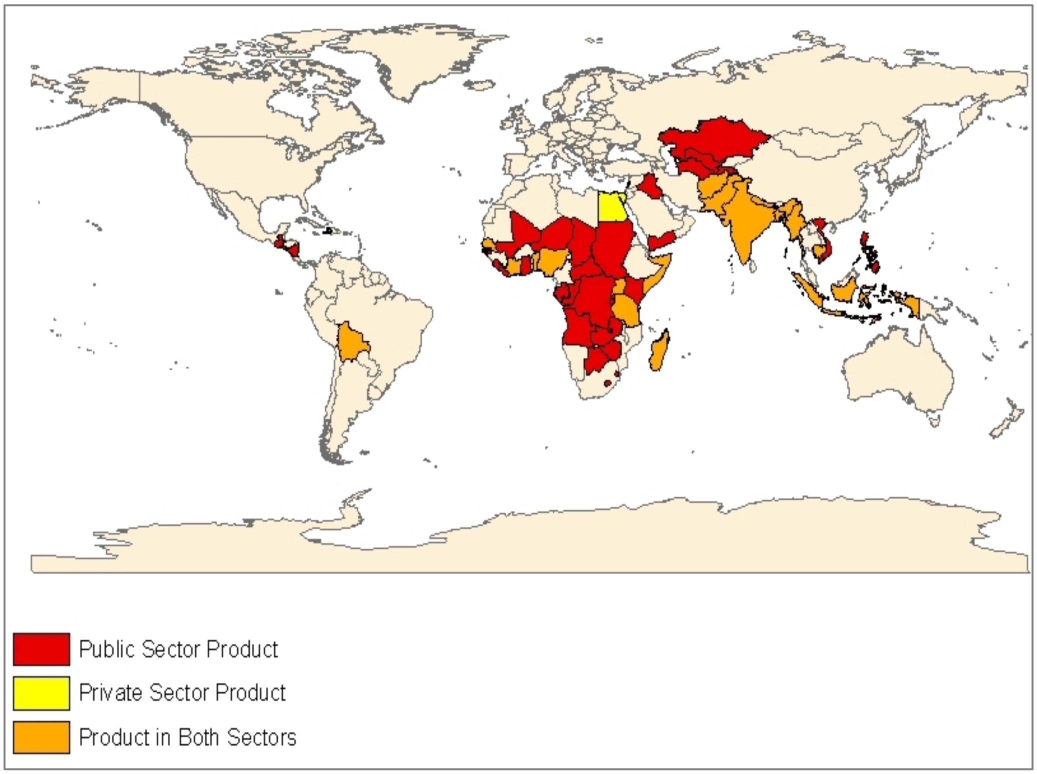
Countries with diarrhea management policies that include zinc, 2011



Source: Zinc Task Force; Personal correspondence with Christa Fischer-Walker, PhD, JHSPH, 2011.

Figure 1.4

Countries with diarrhea treatment products in public, private, or both sectors, 2011



Source: Zinc Task Force; Personal correspondence with Christa Fischer-Walker, PhD, JHSPH, 2011.

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Chapter Two: Methods

2.1 Introduction

The research described in this dissertation was conducted in collaboration with the Johns Hopkins University Institute for International Programs (JHU IIP) and the Society for Applied Studies (SAS). Dissertation research activities were nested within a large-scale effectiveness evaluation of diarrhea management programs in Uttar Pradesh (UP), Gujarat and Bihar, India.

The findings of this dissertation were divided into three papers. Paper 1 identified and discussed the household- and village-level influences of diarrheal illness, care-seeking and treatment among children under-five. Paper 2 determined the degree to which diarrheal severity motivated recall, care-seeking and treatment of episodes among caregivers of children under-five. Paper 3 evaluated the association between knowledge and observed ORS/zinc prescribing practices among providers in the public and private sectors. The following chapter describes the study sites and provides an overview of the methodology employed for the overarching evaluation, as well as each of the three papers.

2.2 Study Sites

Research activities were conducted in Bihar, UP and Gujarat, India on a population of children 2-59 months of age, as well as caregivers and healthcare providers of such children. These three states represent the Central (UP), East (Bihar) and West (Gujarat) regions of India (Figure 2.1) [1]. Though the burden of under-five mortality and diarrhea are high across all three states (Table 2.1), Gujarat has higher GDP per capita and lower under-five mortality compared to UP and Bihar [2, 3].

According to the National Family Health Survey-3 (NFHS-3), the two-week prevalence of diarrhea among children under-five was 9% across India, 8% in UP, 11% in Bihar, and 13% in Gujarat in 2006 (Table 2.1) [4-7]. In terms of the total number of diarrheal deaths among children under-five, UP, Bihar and Gujarat respectively rank first, second and sixth compared to all 28 states in India [3]. Of the estimated 257,000 deaths attributable to diarrhea among Indian children under-five in 2007, approximately 69,451, 28,958 and 11,960 occurred in UP, Bihar and Gujarat, respectively [3].

Despite guidelines by the Government of India and the Indian Academy of Pediatrics (IAP) promoting adequate treatment of diarrhea among children under-five [8, 9], health facility care was sought for only 60% of episodes in 2006 and coverage of ORS (26%) and zinc (0.3%) was low across India [10]. During the same time period, ORS coverage was 13% in UP, 21% in Bihar and 26% in Gujarat [4-6].

2.3 JHSPH Evaluation Study

2.3.1 Evaluation Background

In the fall of 2010, the Bill and Melinda Gates Foundation (BMGF) contracted JHU IIP and, India-based partner, the Society for Applied Studies (SAS) to conduct a large-scale effectiveness evaluation of the Diarrhea Alleviation through Zinc and ORS Treatment (DAZT) program in selected districts of Uttar Pradesh and Gujarat, India. With the overall goal of decreasing diarrhea-associated morbidity and mortality among children under-five in India, the DAZT program was designed to focus on ORS and zinc promotion through both the public and private sector channels. The Children's Investment Fund Foundation (CIFF) pledged support for a similar program that solely targeted the public sector in selected districts in the state of Bihar and also contracted IIP and SAS to implement evaluation activities. Micronutrient Initiative (MI) was responsible for procuring product and implementing ORS and zinc scale-up activities in the public sectors of all three states. FHI 360 was responsible for private sector activities in UP and Gujarat (Figure 2.1).

The states of UP, Gujarat and Bihar were selected for program implementation because of the high burden of diarrhea among children under-five combined with logistical opportunities to leverage momentum surrounding child survival. In each state, specific project districts were selected in consultation with the state governments and the National Rural Health Mission (NRHM) to ensure the geographic, economic, and social representativeness of the sample. Furthermore, the inclusion of the NRHM in program planning was strategic, since the NRHM is positioned to incorporate successful aspects of these state-specific diarrhea management programs into future ORS and zinc scale-up initiatives implemented throughout the country. Program implementation was planned for 12, 6 and 15 districts in UP, Gujarat and Bihar, respectively (Figure 2.1).

The long-term goal of the DAZT project in UP/Gujarat and the CIFF project in Bihar was to reduce the burden of childhood diarrhea in the selected states. Within an allotted three-year timeframe, the project aimed to achieve the following objectives in select implementation districts:

1. increase the demand for ORS and zinc among providers and caregivers of children under-five;

2. increase the availability of ORS and zinc products to providers and caregivers;
3. and demonstrate the cost-effectiveness and logistical feasibility of ORS and zinc scale-up for future mainstream expansion into districts and states not included in the given project.

Program activities implemented by MI in all three states were intended to address the supply and demand barriers existent in the public sector. The primary objective of the public sector arm of the project was to create a sustained and adequate source of ORS and zinc through government health channels while enhancing effective distribution and utilization. While a lower proportion of caregivers of children under-five seek care for diarrhea through the public compared to private sector, the program was designed on the basis that increased availability and improved quality of government services would increase the utilization of diarrhea treatment through this channel. Public sector implementation was thus centered on the following seven key activities.

1. *Provision of advocacy and technical assistance.* Project implementers encouraged the inclusion of zinc and ORS in the NRHM's state-level plans and provided technical assistance for effective and cost-effective scale-up of ORS and zinc at district- and state-level.
2. *Procurement of ORS and zinc and provision of supply chain support*. MI worked with Healthy Life Pharma Pvt. Ltd. to design an ORS-zinc combination packet containing two ORS sachets, 14 dispersible 20 mg zinc tablets, a small cup in which to dissolve the zinc tablets in water or milk, and an illustrated instructional pamphlet. MI procured seed supplies of these ORS-zinc combination packets for distribution in all program districts during the first year of project implementation,

as per the MI supply chain (Figure 2.2). MI subsequently transferred the responsibility of procurement and distribution to the individual state governments, providing continued technical assistance to ensure a smooth transition and supply chain sustainability.

3. *Capacity building of frontline workers and volunteers*. MI contracted external organizations to conduct diarrhea management trainings for government-employed providers with roles in the treatment of diarrhea among children under-five years of age (i.e. medical officers, auxiliary nurse midwives, Anganwadi workers (AWWs), and Accredited Social Health Activists (ASHAs)). The external training organizations included New Concept Information Systems in Bihar; TRIOS Development Support in Gujarat; and Hindustan Latex Family Planning Promotion Trust in UP.
4. *Formative research and development of appropriate messages*. MI utilized WHO guidelines on formative research to gauge barriers to behavior change and to develop and prioritize key ORS and zinc promotional messages for providers and caregivers of children under-five.
5. *Dissemination of messages through various delivery channels*. In collaboration with FHI 360, MI consulted local communications specialists to determine the channels through which the delivery of key provider and caregiver messages would be most effective.
6. *Provision of interpersonal communication (IPC) for providers and caregivers.* MI distributed IPC tools to trained ASHAs and AWWs to aid them in instructing

caregivers on ORS and zinc preparation. IPC tools included pictorial cards, diagrams and flip charts.

7. *Strengthening monitoring of diarrhea management to ensure project sustainability*. MI project managers at district and sub-district levels conducted regular field visits to gather information for evidence-based problem solving. Regular monitoring and program reviews were conducted to encourage project fine-tuning.

In the private sector, the program aimed to increase the demand and utilization of ORS and zinc among private providers in UP and Gujarat. FHI 360 activities were targeted to both formal private sector providers, such as pediatricians and general practitioners, and informal private sector providers, such as rural medical practitioners (RMPs) and rural chemists. FHI 360 was responsible for implementing the following five key activities.

1. *Formative research and development of appropriate messages*. FHI 360 collaborated with MI to develop effective behavior change communication for both caregivers and private sector providers. Formative research included outreach to informal providers to ensure that messages resonated with RMPs and rural pharmacists.
2. *Promotion of zinc and ORS among formal private sector providers*. FHI 360 pushed forward the topic of ORS and zinc treatment for childhood diarrhea at interactive meetings and conference sessions with the UP and Gujarat chapters of the Indian Academy of Pediatrics (IAP) and the Indian Medical Association (IMA). FHI 360 also leveraged existing relationships with pharmaceutical

partners and tasked them with soliciting the sale of zinc supplies to formal private sector providers.

3. *Promotion of zinc and ORS among informal private sector providers*. Expanding upon an existing USAID-funded project known as Naya Daur, FHI 360 organized repeat visits to informal private sector providers by local NGO staff during which adequate diarrhea management was encouraged and zinc samples were distributed. Utilization of indigenous NGOs raised the potential for project sustainability.
4. *Ensured access to ORS and zinc supplies among informal private sector providers*. Given the absence of zinc production and distribution in rural India, FHI 360 collaborated with local pharmaceutical companies to solicit zinc supplies, helping to ensure sustained access.
5. *Creation of zinc and ORS demand among caregiver of children under-five*. FHI 360 conducted demand generation activities, including media campaigns and community-level discussions.

2.3.2 Evaluation Study Design

The main objective of the JHU IIP/SAS evaluation was to measure changes over time in the use of ORS and zinc to treat diarrhea among caregivers and providers of children under-five in UP, Gujarat and Bihar. The evaluation had a prospective, quasi-experimental, pre-post design. The design was quasi-experimental because the states and districts in which program activities were implemented were not randomly selected but rather strategically chosen to represent a high burden of childhood diarrhea and to ensure geographical, social, and economic representativeness. Furthermore, randomization of geographic areas to program or control would not have been logistically feasible given that state-level government plans to introduce zinc at scale could have contaminated areas outside the program area, precluding such regions from serving as controls. Consequently, a pre-post design which made use of historical control areas to test the counterfactual was most appropriate.

2.3 Overview of Data Collection

2.3.1 Baseline data collection for Papers I and II and midline data collection for Paper II

Baseline household coverage surveys were conducted in all program districts from May to June, 2011 in Bihar and from March to June, 2011 in Gujarat and UP (Figure 2.1). Midline household coverage surveys were not carried out in Bihar due to CIFF budget constraints but were conducted from September to October, 2012 in Gujarat and UP (Figure 2.1); data collection at midline was restricted to districts in which ORS and zinc were available through the MI supply chain and public sector health workers had received MI diarrhea management training (i.e. 4 districts in Gujarat and 8 districts in UP; Figure 2.1).

Table 2.2 outlines the sample sizes achieved at each phase of data collection. For the baseline surveys, sample size requirements were calculated at the state-level to detect the proportion of children 2-59 months of age that had experienced diarrhea in the two weeks prior to the survey and had been treated with ORS. For the midline surveys, required sample sizes were calculated to detect a change in this proportion since baseline with 80% power at the alpha=5% level.

In each state and for all surveys, the total required sample size was divided evenly across included districts. Researchers used the 2001 Indian census and Stata statistical software to generate a systematic random sample of rural villages within each district [11, 12]. Trained data collection teams visited households in the first randomly selected village and continued until either a maximum of 50 caregivers of children 2-59 months of age had been enrolled or all households in the village had been visited. The team continued to visit villages and households sequentially until the desired sample size was met.

Trained interviewers administered the questionnaire to consenting primary caregivers of children 2-59 months of age. The questionnaire ascertained sociodemographic and socioeconomic information, as well as diarrhea management knowledge and practices. Extended questions on care-seeking and treatment were administered to caregivers of children that had experienced a diarrheal episode in the two-weeks prior to the survey.

2.3.2 Provider assessment data collection for Paper III

Cross-sectional provider assessments were conducted from October to November, 2011 in Bihar; December, 2011 to January, 2012 in Gujarat; and June to July, 2012 in UP. Data collection was carried out in all districts in which the first phase of the program had been implemented and included 5 districts in Bihar, 4 districts in Gujarat and 12 districts in UP. The provider assessments focused on informal private sector RMPs in UP and public sector ASHAs and AWWs in Bihar and Gujarat.

A multi-stage cluster sampling design was employed in which the primary sampling unit was the primary health center (PHC) in the public sector and the tehsil, a geographic entity, in the private sector. In each district, PHCs/tehsils were randomly selected based on a probability proportional to size (PPS) sampling design, such that the proportion of sampled PHCs/tehsils equaled the proportion of PHCs/tehsils in that district relative to the total across all districts included in the assessments for a given state. The required sample sizes of providers were calculated to detect: 1) the proportion of ASHAs/AWWs that prescribe ORS to treat diarrhea in Bihar and Gujarat and 2) the proportion of RMPs that prescribe zinc to treat diarrhea in UP. ORS was used as the basis for public sector sample sizes because zinc was not widely accessible prior to program implementation; however, zinc was used for the private sector because ORS prescribing was not common among RMPs. The required sample sizes of providers were randomly selected from the PPS samples of PHCs/tehsils.

Data collection consisted of two components: 1) direct observation of the provider during consultation with one eligible diarrhea case and 2) an administered questionnaire. In order to identify children eligible for direct observation (i.e. 2-59 months of age, experiencing a current, untreated episode of three or more loose/watery stools in the preceding 24 hours), trained data collectors waited for one working day at RMP practices and accompanied ASHAs and AWWs during routine community visits. During the direct observations, interviewers took note of whether providers questioned caregivers about diarrheal severity and provided or recommended any course of treatment. After the observation, interviewers administered the questionnaire, which gauged diarrhea management knowledge and practices and access to ORS and zinc supplies.

2.3.3 Endline coverage surveys

Endline coverage surveys of all program districts took place from September-December 2013 in Bihar and Gujarat and are planned for September-October 2014 in UP. Data collection methods were designed to mimic those employed at baseline and midline. These data will inform the overarching evaluation on changes in household knowledge and utilization of ORS and zinc for the treatment of diarrhea among children 2-59 months of age. Endline data was not used for completion of the objectives described in this dissertation.

2.4 Overview of Statistical Methods

2.4.1 Overview of statistical methods for Paper 1

Baseline data from UP and Gujarat were employed to perform multilevel data analyses assessing the effects of household- and village-level covariates on each of three outcomes: 1) the occurrence of diarrhea among children 2-59 months of age in the two-weeks preceding the survey; 2) care-seeking outside the home and 3) ORS treatment for a reported diarrheal episode in the two-weeks prior to the survey. For each outcome, four sets of multilevel logistic regression models were fitted using data from the baseline household coverage surveys in UP and Gujarat. The analyses were performed in Stata 12.0 using adaptive Gaussian quadrature with 12 integration points and accounting for the survey sampling weights of households and villages [11]. All models fit a random intercept for village to account for inter-village variation in the baseline odds of the outcomes. In addition to the random intercept, model 2 included fixed effects for household-level covariates, and model 3 included fixed effects for both household- and village-level covariates. Model 4 was fitted by adding random slopes for household-level covariates to model 3, which allowed for effect sizes to vary by village in addition to the baseline odds of the outcome. Data from Bihar were not included in Paper 1 because costing analyses were not planned in this state, and therefore, it was not possible to calculate pertinent predictor variables for household- and village-level wealth using Bihar data.

2.4.2 Overview of statistical methods for Paper II

The objective of this analysis was to assess the influence of diarrheal episode severity on caregiver recall, care-seeking and ORS/zinc treatment for diarrhea among children under-five. Using baseline and midline survey data from UP, Gujarat and Bihar, binary outcome variables were generated to indicate 1) whether reported onset of diarrhea had occurred 7-14 days as opposed to 3-6 days prior to the survey; 2) whether care had been sought outside the home through any source; and 3) whether the episode had been treated with ORS/zinc. Logistic regression models were fitted for the log odds of each outcome with the robust cluster estimator of variance in Stata 12.0 [11]. The saturated models included explanatory variables for symptoms of the diarrheal episode, such as duration, blood in stools, dehydration, maximum stool frequency (stools/day), fever, and vomiting. A multinomial logistic regression model was fitted for a categorical dependent variable for whether care was sought through the public sector alone, private sector alone, or both sectors.

2.4.3 Overview of statistical methods for Paper III

The goal of this analysis was to assess the association between observed prescribing practices for childhood diarrhea and reported knowledge of ORS and zinc treatment among RMPs, ASHAs and AWWs in UP, Gujarat and Bihar. Principal components analysis (PCA) was conducted on variables generated from the provider assessment survey responses in order to construct three indexes: 1) zinc knowledge index; 2) ORS knowledge index; 3) combined zinc and ORS knowledge index. Logistic regression analysis with the robust cluster estimator of variance was employed in Stata 12.0 to model the log odds of observed zinc prescribing, the log odds of observed ORS prescribing and the log odds of observed ORS and zinc prescribing as a function of the relevant knowledge index score [11]. For all outcomes, models also included relevant explanatory variables, such as years of education, whether the provider had received diarrhea management training in the six months prior to the survey, and whether the provider had access to ORS/zinc stocks at the time of the survey.

2.5 Ethical Considerations

Research activities were reviewed and approved by the Johns Hopkins University Bloomberg School of Public Health Institutional Review Board (IRB Numbers 3390 and 3530) and by the Society for Applied Studies Ethical Review Committee in New Delhi, India. Written informed consent was obtained from all surveyed study participants, including providers and caregivers of children. Verbal assent was obtained from the caregivers of children observed in consultation with providers. Illiterate individuals were asked to provide a fingerprint in lieu of a signature to indicate their consent. Each participant was provided with a copy of the consent form, which included a local phone number for follow-up questions.

2.6 Data Management and Quality Control

JHU IIP and SAS researchers developed survey instruments and standard operating procedures, outlining specific instructions for survey implementation and form filling. Prior to each round of data collection, the data collection team gathered in New Delhi for a 3-day training session led by SAS researchers. Trainings included classes, mock interviews, form filling, and a review of the logistics of daily field operations. Difficulties with the survey instruments were also identified and addressed during training activities. The data collection team was taught to protect the privacy of individuals and to maintain the confidentiality of all personal identifiers.

Mindfield Research was contracted to hire staff fluent in local dialects, organize transportation within and between districts, and oversee the quality and logistics of data collection. Coordinators were trained to check data collection forms for accuracy nightly, and inconsistencies were resolved in the field. Technical issues were communicated to SAS researchers in Delhi on a daily basis, and difficulties were addressed in a timely fashion. Data collection forms were photocopied in the field and hand-delivered to the SAS office in New Delhi where data were entered into predesigned databases. SAS researchers conducted checks for inconsistencies and logical errors and cleaned the electronic data.

Table 2.1

Child survival statistics by state

State	Mid-year Population, 2007 [a]	Under-5 Mortality Rate [a]	Estimated Under-5 Deaths, 2007[a]	Infant Mortality Rate [a]	Neonatal Mortality Rate [a]	Two-week Diarrhea Prevalence (%) [b]
Bihar	92,699,000	76	206,849	58	31	11
Gujarat	56,088,000	66	84,425	52	37	13
UP	187,928,000	89	496,077	69	48	8

Sources: **[a]** Lahariya C, Paul VK: Burden, differentials, and causes of child deaths in India. Indian J Pediatr 2010, 77(11):1312-1321 [3].

[b] IIPS (International Institute for Population Sciences) and Macro International: National Family Health Survey (NFHS-3), 2005-06, India: Key Findings. In. Mumbai: IIPS; 2007[10].

Table 2.2

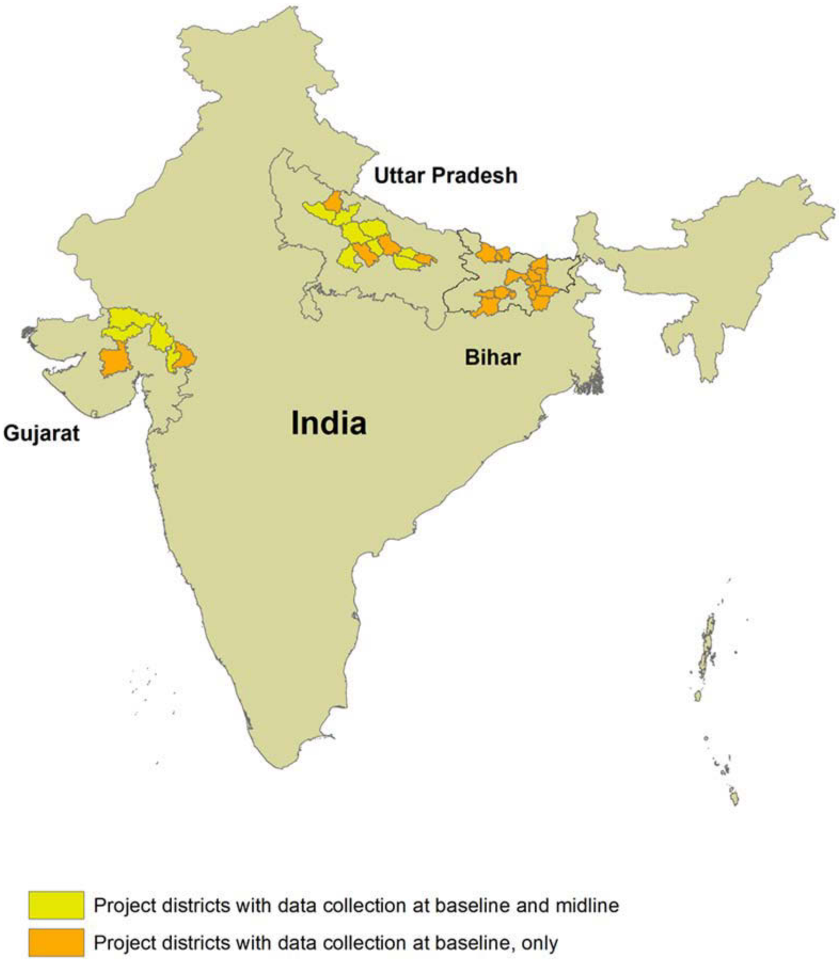
Sample sizes achieved in each state at baseline and midline

State	Survey	Surveyed households with child 2-59 months of age	Surveyed households with child 2-59 months of age and diarrhea in the two-weeks prior to the survey
Bihar[a]	Baseline	2,645	437
Gujarat	Baseline	4,200	594
	Midline	1,072	165
UP	Baseline	3,889	652
	Midline	1,790	284
Total		13,596	2,132

[a] Midline surveys were not conducted in Bihar.

Figure 2.1

Map of diarrhea management program activities by state and district [a, b]



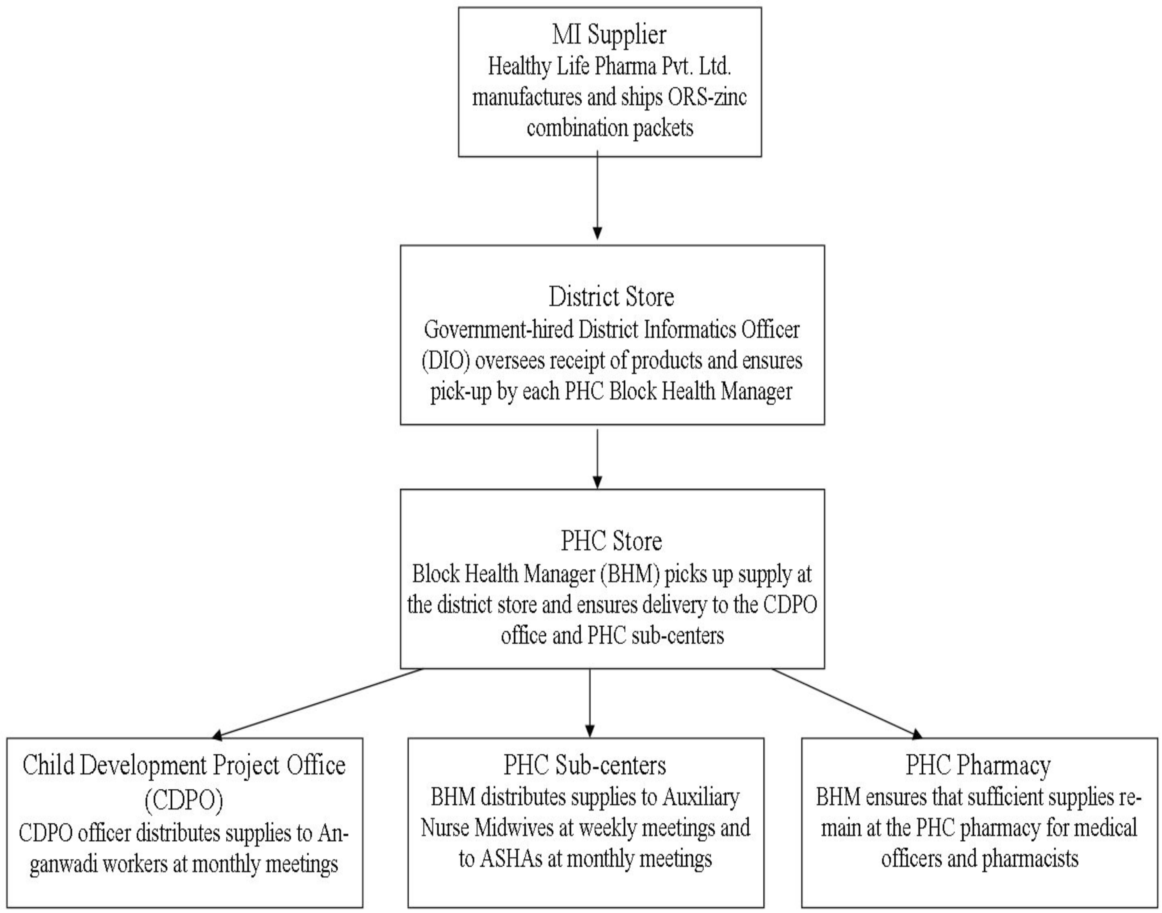
Source: Map was generated using ArcGIS software and DIVA-GIS shapefiles [13, 14].

[a] Data collection at baseline and midline in 8 districts in UP (*Badaun, Faizabad, Hardoi, Kanpur Dehat, Lucknow, Shahjahanpur, Sitapur, Sultanpur*) and 4 districts in Gujarat (*Banas Kantha, Panch Mahals, Patan, Sabar Kantha*). Data collection at only baseline in 15 districts in Bihar (*Banka, Bhagalpur, East Champaran, Gaya, Jehanabad, Khagaria, Madhepura, Munger, Nalanda, Saharsa, Samastipur, Sheikhpura, Sheohar, Sitamarhi, Supaul*), 4 districts in UP (*Ambedkar Nagar, Bara Banki, Bareilly, Unnao*) and 2 districts in Gujarat (*Dohad, Surendranagar*).

[b] Program implemented in the public and private sectors of Gujarat and UP and the public sector alone in Bihar.

Figure 2.2

MI supply chain for procurement and distribution of ORS-zinc combination product in the public sector



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Chapter Three: Paper 1

Multilevel determinants of diarrheal illness, care-seeking and treatment among children 2-59 months of age in Uttar Pradesh and Gujarat, India

3.1 Introduction

3.1.1 The burden of diarrhea among children under-five

Diarrhea is the third leading cause of death among children under-five globally, after pneumonia and pre-term births [1]. In 2011, 711,800 deaths among children under-59 months of age were attributable to diarrhea [2]. Approximately one-fourth of under-five diarrheal deaths occur in India—the country with the highest burden of childhood diarrhea in the world [1]. Diarrheal mortality is high across India and, specifically, in the states of Uttar Pradesh (UP), Gujarat, and Bihar, which as of 2007 accounted for approximately 27%, 5% and 11% of the annual under-five diarrheal deaths in India, respectively [3].

Diarrhea is responsible for significant childhood morbidity in low- and middle-income countries worldwide. In 2010, an estimated 1.731 billion episodes of diarrhea occurred in children under-five globally [2]. For the same time period, global diarrhea incidence was 2.9 episodes per child <59 months of age per year, and in India, the respective age-specific diarrhea incidence rates were 2.50, 3.82, 3.09 and 1.98 episodes/child-year among children 0-5, 6-11, 12-23 and 24-59 months of age [4].

Approximately 2% of diarrheal episodes progress to severe illness, and the global case-fatality ratio for such episodes is 2% (uncertainty range: 1.4-4.4%) [2]. However, even among children with mild or moderate episodes that do not progress to death, repeated bouts of diarrhea per year can result in long-term sequelae, such as poor nutritional status, stunting and subsequent decreases in cognitive function [2, 5, 6].

3.1.2 Risk factors for diarrhea among children under-five

Several nutritional determinants have been established as important risk factors for diarrhea among children under-five years of age. Children with poor nutritional status as indicated by anthropometric measures, such as weight-for-age (underweight), weight-for-height (wasting) and height-for-age (stunting), are at increased risk of diarrheal illness and episodes of longer duration [2, 7-13]. The burden of diarrhea is elevated among children deficient in zinc [14], and deficiencies in zinc and Vitamin A increase the risk of severe diarrhea and mortality [13-15]. In addition, children with suboptimal breastfeeding during the first two years of life are at higher risk of incident and prevalent diarrhea, as well as diarrhea-attributable hospitalizations and mortality [13, 16].

Given that diarrheal pathogens are predominantly transmitted via the fecal-oral route through ingestion of contaminated food or water, limited access to clean water, poor sanitation, and inadequate personal hygiene are significant risk factors for childhood infections [17-20]. As such, hand washing with soap, improved water quality and safe disposal of human excreta are associated with reductions in childhood morbidity due to diarrhea [20].

Unimmunized children are at increased risk for vaccine-preventable diarrheal infection and death. Even moderate coverage of the vaccine for measles, which is a risk factor for measles-associated diarrhea, has been shown to decrease diarrhea incidence and mortality in children younger than five years of age [21]. The cholera and rotavirus vaccines could potentially prevent one-third of the global burden of vaccine-preventable diarrheal episodes among children under-five [2].

In addition, there are distal risk factors for diarrheal morbidity and mortality, which include determinants of wealth and development, such as low socioeconomic status (SES), lack of maternal education, maternal illiteracy, crowding and residence in a rural area or urban slum [22-27].

3.1.3 Factors influencing care-seeking and ORS treatment for diarrhea among children under-five

Oral rehydration salts (ORS) are recommended, in combination with zinc supplementation, for the treatment of diarrhea among children under-five globally and in India [28-30]. However, despite formal recommendations and lifesaving impact, ORS coverage has stagnated (or declined) over the past decade [31, 32]. Studies have established that ORS use is often low even in communities where knowledge of the existence of ORS is high [33]. Factors influencing the use of ORS include child age, episode severity and duration, household SES and maternal education [33-35]. Provider recommendation also impacts ORS use [33, 35], highlighting the importance of seeking care outside the home for all diarrheal episodes among children under-five. In addition, maternal education and household SES have been linked to increases in care-seeking for diarrhea among caregivers of children under-five years of age [34], as well as increases in healthcare utilization in general [36].

3.1.4 Assessing the contextual determinants of diarrheal illness, care-seeking and ORS treatment beyond the household-level

There is mounting evidence that diarrheal illness, care-seeking and treatment are not solely influenced by characteristics of the individual but also by variables defined at the community-level [34, 37-39]. Hierarchical models designed to assess the individual and contextual influences of diarrheal duration and care-seeking have concluded that such outcomes are influenced by both household wealth and the overall level of economic development within the community [34, 37]. In addition, collective measures of education and social support at the population-level have influenced the use of ORS among women in both rural and urban communities [38]. Multilevel analyses have also demonstrated a protective effect of community-level sanitation even after controlling for household practices surrounding hygiene, food preparation and excreta disposal [37, 39].

Identification of the determinants that most closely influence diarrheal illness, care-seeking and treatment among children under-five years of age is integral to the success of diarrhea management programs and evaluations of such programs. Programs may benefit from knowledge of the relative importance of household- and community-level influences on key outcomes. This study sought to assess the household- and village-level determinants of diarrheal disease, care-seeking and treatment using baseline data from the large-scale evaluation of the Diarrhea Alleviation through Zinc and ORS Treatment (DAZT) program in Gujarat and UP, India. The main goal of the DAZT program was to scale-up oral rehydration salts (ORS) and zinc supplementation for the treatment of diarrhea among children under-five. Scale-up activities were implemented by Micronutrient Initiative (MI) in the public sector and by FHI 360 in the private sector.

The program evaluation was designed and implemented by the Johns Hopkins University Institute for International Programs (JHU IIP) and in-country partner, the Society for Applied Studies (SAS). Although JHU IIP and SAS simultaneously evaluated a similar program in Bihar, the data from this state excluded household asset variables pertinent to the analysis and were therefore not utilized in the study described in this chapter.

3.2 Methods

3.2.1 Sample size requirements for the overarching evaluation

Sample size requirements for baseline data collection were calculated in Stata 10.0 to allow 80% power to detect ORS coverage of 26.3% ± 18.7% in Gujarat and 16.5% ± 16.5% in UP at the alpha=5% level [40]. For each state, the required sample size was adjusted to allow adequate power to detect ORS coverage among the poorest two wealth quintiles and to account for inter-household correlation, missing observations, and two-week diarrhea prevalence. Adequate power to detect zinc coverage was not a concern at baseline because zinc scale-up had yet to take place and coverage was very low. The required sample size for the baseline household coverage survey was 4,167 and 3,889 caregivers of children 2-59 months of age in Gujarat and UP, respectively.

3.2.2 Sampling Design

Baseline data were collected from 6 districts in Gujarat and 12 districts in UP (Figure 3.1) using a systematic sampling design. The sample size required for each state was divided evenly across the included districts such that the district-required sample sizes were roughly 695 caregivers per district in Gujarat and 324 caregivers per district in

UP. A list of rural villages within each district was generated from the 2001 government census data and randomly rank-ordered using Stata 10.0 [40, 41]. In each district, the data collection team visited villages in rank order until the district-required sample size was obtained.

In order to randomly select households within a given village, a trained data collection team coordinator divided the geographic area into four quadrants and split the team accordingly. Once situated within their assigned quadrants, data collectors selected a central location and proceeded to visit households to the right of that location. For each village, this process was repeated until all village households were visited or a maximum of 50 caregivers of children 2-59 months of age had been interviewed.

3.2.3 Interviewer Training

The data collection team was trained at SAS headquarters in New Delhi before implementation of field activities. SAS researchers instructed the team on how to correctly administer questions and fill survey forms. The logistics of field operations were also thoroughly reviewed with the team supervisors responsible for overseeing survey implementation and refresher trainings while in the field.

3.2.4 Ethical Approval

The Johns Hopkins University Institutional Review Board (IRB) in Baltimore, MD and the Society for Applied Studies Ethical Review Committee (ERC) in New Delhi, India granted ethical approvals for this study. Data collectors obtained informed consent from all study participants (i.e. caregivers of children 2-59 months of age agreeing to the survey). The consent forms were translated from English into Hindi/Gujarati and subsequently back-translated into English to ensure correctness. Participating caregivers were asked to indicate their consent with a signature or with a thumbprint and witness signature if illiterate.

3.2.5 Data Collection

The baseline cross-sectional household survey was administered from March-June 2011. The data collection team visited households as per the sampling scheme outlined in section 3.2.2 in order to identify those with children 2-59 months of age in residence. Primary caregivers of at least one child 2-59 months of age were considered eligible for inclusion in the study; primary caregivers were typically mothers but in some households a grandmother or aunt held this role due to a mother's death. Caregivers of more than one child in the inclusive age range were asked to focus their survey responses on the youngest child. In multi-family (i.e. joint family) households, a maximum of one eligible caregiver was enrolled in the study.

The survey lasted about 20-30 minutes and was administered in Hindi in UP and Gujarati in Gujarat. Questions on general diarrhea management knowledge and practices, demographics and asset ownership were administered to all participants. A second set of questions on recent episode symptoms, care-seeking and treatment practices were only administered to caregivers of children that had experienced a diarrheal episode in the two weeks prior to the survey.

3.2.6 Quality Control

Data collection team coordinators inspected forms on a daily basis and addressed inaccuracies before moving the team to the next village. Forms were transported to SAS headquarters in New Delhi where they were double data entered into predesigned databases. SAS researchers cleaned the data and consulted with coordinators situated in the field in an effort to resolve any additional errors or logical discrepancies uncovered during data entry and cleaning.

3.2.8 Data Analysis

The goal of this analysis was twofold: 1) to identify the household- and village-level determinants of diarrhea occurrence among children under-five and 2) to identify the household- and village-level determinants of care-seeking and ORS treatment among children under-five with diarrhea. The analysis was designed to assess variation in the prevalence of diarrhea and in the coverage of careseeking and ORS treatment for diarrhea across randomly selected households and rural villages.

Three binary outcome variables were generated using survey data on: 1) the occurrence of diarrhea during the two-weeks preceding the survey, 2) care-seeking for two-week diarrheal episodes; and 3) ORS treatment of two-week diarrheal episodes. Exploratory data analysis was performed to quantify inter-household variation in the three outcomes.

The three outcome variables were aggregated across villages in order to generate village-specific estimates of two-week diarrhea prevalence, coverage of diarrhea care-seeking, and coverage of ORS treatment for diarrhea. Inter-village variation in the three outcomes was assessed through exploratory data analysis of the village-specific prevalence and coverage estimates.

Multilevel data analysis was employed to assess the effects of household-level and village-level covariates on each of the three outcomes. This method of analysis allowed for consideration of the hierarchical nature of the data—households (level 1) nested within villages (level 2). It is important to note that the household-level includes covariates describing both the attributes of included children and their primary caregivers and that the decision to group these covariates into one household-level was based on knowledge of the study design, which permitted inclusion of a maximum of one child-caregiver pair per household; in the event that multiple children and/or caregivers were enrolled per household, data analysis would have taken into account an additional level for children nested within households nested within villages.

Four multilevel logistic regression models were fitted separately for the log odds of each outcome. For each outcome, model 1 fit a random intercept for village; model 2 fit a random intercept for village and fixed effects for household-level covariates; and model 3 fit a random intercept for village and fixed effects for both household-level and village-level covariates. For all outcomes, several iterations were constructed for model 4, which fit a random intercept for village and a random slope for the statistically significant household-level covariates in model 3. In all models, the random intercept for village allowed for the baseline log odds of the outcome (i.e. βo, the value of the outcome in the presence of no explanatory variables) to vary by village. In model 4, the random slopes included for various covariates allowed for the effect of those covariates on the outcome variable to vary by village. The equations for each model are as follows:

Model 1: $logit(p_{ik}) = \beta_{o_k}$

Model 2: $logit(p_{ik}) = \beta_{o_k} + \beta_1 x_{ik}$

Model 3: $logit(p_{ik}) = \beta_{o_k} + \beta_1 x_{ik} + \beta_2 x_{ik}$

Model 4: $logit(p_{ik}) = \beta_{o_k} + \beta_{1_k} x_{ik} + \ \beta_2 x_{ik}$

For a given outcome, p_{ik} is the probability of that outcome in household i nested within village k; $logit(p_{ik})$ signifies the log odds of that outcome; β_1 and β_2 represent vectors of beta coefficients for household- and village-level covariates, respectively; x_{ij} is a vector of the explanatory covariates included in the model; and $\beta_{o_k}$is the random intercept for village k, which is assumed to be normally distributed with mean 0 and constant variance = σ_k^2 in models 1-3. The null hypothesis that σ_k^2 = 0 is tested in order to assess whether the log odds of the outcome are correlated between households (level 1) and villages (level 2); if the 95% confidence interval for the random intercept variance overlaps zero, the random effect is not necessary and the model reduces to a typical logistic regression model [42]. The β_{1_k} included in model 4 represents the random slopes of included household-level covariates for village k. In model 4, the random intercept and slope are assumed to be multivariate normally distributed with mean 0, intercept variance = σ_{0k}^2, slope variance = σ_{1k}^2 and covariance = τ_{o1}. The null hypothesis that the random slope variance equals zero is used to assess whether the effect of a given covariate on the log odds of the outcome differs by village. Following these criteria, the statistical significance of random intercept and random slope terms were assessed for all outcomes.

All models were fitted in Stata 12.0 using adaptive Gaussian quadrature with 12 integration points and accounting for the survey sampling weights of households and villages [43]. For each outcome, the household- and village-level covariates considered for inclusion in models 2-4 are described in Table 3.1. Bivariate analyses, Wald statistics and confidence intervals were used to assess the inclusion of individual covariates in final models and to draw inferences for fixed effects.

Household-level variables were constructed from survey responses and included child gender and age, caregiver age and educational attainment, and whether the child's family was in possession of a BPL card indicating below poverty wealth status. Variables for wealth index score and wealth quintile were also included at the household-level; these variables were generated by performing principal components analysis (PCA) on binary indicators of whether the household owned a set of assets (e.g. television, refrigerator) using previously published methods [44]. For models of the log odds of diarrhea, additional household-level variables assessing known diarrhea risk factors were also considered for inclusion (i.e. hospital admission in the previous 3 months, family type (joint or nuclear), family size (total number of persons), number of residents under-five years of age, time to obtain drinking water, source of drinking water, purification of drinking water, and toilet/latrine access) (Table 3.1). Models of the log odds of care-seeking included a covariate for whether the child had recovered from the diarrheal illness by the time of the survey or had experienced loose/watery stools in the 72-hours beforehand, and a covariate for the episode duration in days, which was defined as the difference between reported dates of onset and recovery for recovered children and as the difference between the dates of onset and the survey for children with current episodes (Table 3.1). Variables for episode recovery and duration, care-seeking through any sector, and public sector care-seeking were considered for inclusion in the models of the log odds of ORS (Table 3.1). Interactions of household-level covariates, such as age and duration, were also tested for potential inclusion in the final models using Wald tests of statistical significance.

Village-level variables were generated by aggregating household-level variables across villages (i.e. calculating village-specific means for continuous variables and village-specific proportions for binary variables, such that the value of village-level variables differed by village but was equal for all households within a given village). The following village-specific variables were considered for inclusion in models 3 and 4 for all outcomes: mean wealth index score, proportion of households above the poverty line, mean years of education among caregivers of children under-five, proportion of households in which the primary caregiver of a child under-five has more than primary school education (Table 3.1). The village-specific proportion of households with access to a toilet or latrine was also included in the model of the log odds of diarrhea (Table 3.1).

The compositional effect, which is a term used to describe the extent to which inter-group (i.e. inter-village) variability in an outcome is attributable to differences in the characteristics of individuals (i.e. households) comprising the group [45], was estimated by calculating the percent difference in the variance of the random intercept for village comparing model 2 to model 1. A compositional effect was considered present if the addition of household-level covariates (model 2) to a null model with no covariates (model 1) substantially decreased the random intercept variance, which is a measure of inter-village variability in the outcome.

Model 3 was used to assess the contextual effect of wealth and caregiver education on all outcomes and of toilet/latrine access on diarrhea occurrence. A contextual effect refers to the influence of aggregated group-level (i.e. village-level) variables on outcomes at the individual-level (i.e. household-level) after controlling for relevant individual-level explanatory variables [45]. The contextual effect of a given variable was calculated by subtracting the within group effect from the between group effect of the variable. In model 3, the between group effect was estimated by the beta coefficient for the village-aggregated variable and the within group effect was estimated by the beta coefficient for the household-level variable, which was group-mean centered (i.e. centered on the village mean) to facilitate interpretation. The contextual effect of wealth index score, for example, was determined by comparing the change in the odds of the outcome between two households with the same wealth index score but from villages that differed in village-specific mean wealth index score by one point.

3.3 Results

3.3.1 Characteristics of households and villages

The analysis of diarrhea occurrence included data on 8085 households from 195 villages. The analyses of care-seeking and ORS treatment excluded households in which diarrhea was not reported for a child under-five in the two-weeks preceding the survey and villages in which two-week prevalence of diarrhea was 0% among included children. A total of 1245 households within 185 villages were included in the analyses of the care-seeking and ORS outcomes. There was a median of 50 households per village (IQR: 30-50). The number of households per village ranged from 3-50, with the exception of one village in which 80 households were included due to error on the part of the data collection team.

The two-week prevalence of diarrhea across all households was 15.4% (SD: 36.1%). Among households in which the included child was reported to have experienced diarrhea in the two-weeks prior to the survey, coverage of care-seeking outside the home was 77.9% (SD: 41.5%) and ORS coverage was 18.6% (SD: 39.0%). Table 3.2 describes additional characteristics of included households and children.

Among 195 total villages, the median village-specific diarrhea prevalence was 14.0% (IQR: 9.0-20.0%). The median village-specific coverage estimates of diarrhea care-seeking and ORS treatment were 81.8% (IQR: 66.7-100%) and 16.7% (IQR: 0-30%), respectively, among the 185 villages in which diarrhea was reported for an included child. Figures 3.2-3.4 illustrate the inter-village variation in diarrhea prevalence, care-seeking and ORS treatment. These values are unweighted and therefore influenced by the number of households surveyed per village; multilevel logistic regression analyses were adjusted for sampling weights.

3.3.2 Household- and village-level determinants of diarrhea among children under-five years of age

The variance of the random intercept for village was statistically significantly greater than zero in all models (Table 3.3). There was no evidence of a compositional effect, since the addition of household-level variables (model 2) to the null model (model 1) resulted in only a negligible decrease in the random intercept variance (i.e. -2.86%). In all iterations of model 4, random slopes for the included household-level covariates were not statistically significant and therefore only estimates for models 1-3 are reported (Table 3.3).

From model 3, increased child age (aOR: 0.97; 95% CI: 0.96-0.97) and no hospital admission in the previous 3 months (aOR: 0.29; 95% CI: 0.15-0.52) were protective against the occurrence of diarrhea in a child 2-59 months of age (Table 3.3). The protective effect of household access to a toilet or latrine was modified by caregiver education: the adjusted odds of diarrhea were reduced by 60% among children from households in which the primary caregiver had more than a primary school education (aOR: 0.40; 95% CI: 0.15-1.05) but this reduction was smaller and not statistically significant among children with less educated caregivers (aOR: 0.79; 95% CI: 0.43-1.45) (Table 3.3). Among children whose caregivers were educated beyond primary school, the adjusted odds of diarrhea were reduced if the household had access to a toilet/latrine (aOR: 0.65; 95% CI: 0.42-1.01) but not if the household practiced open defecation (aOR: 1.28 (0.94-1.76) (Table 3.3).

The village-specific proportion of households in which a caregiver of a child under-five had more than primary school education was associated with reduced odds of diarrhea among included children (aOR: 0.34; 95% CI: 0.14-0.82), but the village-specific proportion of households with access to a toilet/latrine was not associated with the outcome (aOR: 1.22; 95% CI: 0.40-3.68) (Table 3.3). There was no evidence of an interaction between village-level education and village-level toilet/latrine access or between household-level and village-level variables for caregiver education and toilet/latrine access.

There was evidence supporting a contextual effect of caregiver education on the occurrence of diarrhea among included children. The odds of diarrhea were 7.4% lower (95% CI: 3.5-8.9%) comparing children from households with the same level of caregiver education but from villages that differed in the village-specific proportion of caregivers educated beyond primary school by 10%.

There was a non-statistically significant trend in reduced adjusted odds of diarrhea per one-unit increase in household wealth index score (aOR: 0.99; 95% CI: 0.95-1.04) and per one-unit increase in village-specific mean wealth index score (aOR: 0.98; 0.84-1.14) (Table 3.3). There was no evidence supporting a contextual effect of wealth on the occurrence of diarrhea among children 2-59 months of age (aOR: 0.98; 95% CI: 0.83-1.16).

3.3.3 Household- and village-level determinants of care-seeking for diarrhea among children under-five years of age

The variance of the random intercept was statistically significant in all models and did not change between models 1 and 2, indicating the absence of a compositional effect (Table 3.4). The random slopes included in model 4 were not statistically significant and were therefore excluded from the results reported in Table 3.4.

From model 3, the adjusted odds of seeking care for an episode of diarrhea in a child 2-59 months of age were associated with episode duration of >3 days (aOR: 2.56; 95% CI: 1.57-4.17), having recovered by the time of the survey (aOR: 3.58; 95 % CI: 2.04-6.29), and residence in UP as opposed to Gujarat (aOR: 8.04; 95% CI: 3.97-16.29) (Table 3.4). There were no statistically significant interactions between any of the included household-level covariates. At the household-level, the adjusted odds of care-seeking were elevated by a factor of 4.10 (95% CI: 1.20-13.98) among caregivers educated beyond primary school (Table 3.4). However, there was no village-level effect of caregiver education on care-seeking (aOR: 0.60; 95% CI: 0.04-9.64) (Table 3.4).

There was no evidence supporting a contextual effect of caregiver education on care-seeking for diarrhea (aOR: 0.15; 95% CI: 0.01-2.88).

Household wealth index score (aOR: 0.86; 95% CI: 0.72-1.05) and village-specific mean wealth index score (aOR: 1.17; 95% CI: 0.86-1.60) had no effect on care-seeking (Table 3.4). There was some evidence for a contextual effect of wealth on care-seeking for diarrhea—comparing two households with the same wealth index score but from villages that differ in mean wealth index score by one point, the adjusted odds of care-seeking were elevated by 36% (aOR: 1.36; 95% CI: 0.95-1.93).

3.3.4 Household- and village-level determinants of ORS treatment for diarrhea among children under-five years of age

The random intercept variance was statistically significant in all models (Table 3.5). Comparing models 1 and 2, there was no decrease in random intercept variance and therefore no compositional effect. Model 4 did not indicate any statistically significant random slopes. The results of models 1-3 are detailed in Table 3.5.

From model 3, the adjusted odds of ORS treatment were higher among children with episodes >3 days in duration (aOR: 1.86; 95% CI: 1.02-3.46) (Table 3.5). Seeking care outside the home through any sector increased the adjusted odds of ORS treatment by a factor of 23 (aOR: 23.74; 95% CI: 7.16-78.78) (Table 3.5). Controlling for whether any care was sought outside the home, seeking care through the public sector had an effect on ORS treatment that was modified by state. In Gujarat, the adjusted odds of ORS treatment were elevated by a factor of 13 among those seeking care through the public sector as opposed to the private sector alone or nowhere (aOR: 13.45; 95% CI: 2.93-

61.73). In UP, there was a non-statistically significant trend in increased odds of ORS among public sector care-seekers (aOR: 1.80; 95% CI: 0.58-5.59) in UP (Table 3.5).

Increased household wealth index was associated with higher odds of ORS treatment (aOR: 1.22; 95% CI: 1.02-1.46) (Table 3.5). The village-specific mean wealth index had no effect on ORS use (aOR: 1.07; 95% CI: 0.76-1.52) (Table 3.5), and there was no evidence of a contextual effect (aOR: 0.88; 95% CI: 0.60-1.30).

There was a non-statistically significant trend in higher odds of ORS treatment among children with more highly educated caregivers (aOR: 1.73; 95% CI: 0.53-5.61) (Table 3.5). Village-level caregiver education had no effect on ORS use (aOR: 2.23; 95% CI: 0.06-79.92) (Table 3.5), and there was no evidence supporting a contextual effect (aOR 1.29; 95% CI: 0.03-57.70).

3.4 Discussion

3.4.1 General findings

In this analysis, multilevel models were used to assess household and village influences on diarrheal illness, care-seeking and ORS treatment. Among children 2-59 months of age, diarrheal illness, care-seeking and ORS treatment were variable by village, even after controlling for household-level predictors and sampling weights. The statistically significant variance of the random intercept for village across all models indicated that village was a meaningful determinant of the odds of each outcome. While village impacted the value of the odds of the outcome when all model covariates were set to zero (i.e. the value of the intercept), the effect sizes of included covariates were not found to vary by village, as indicated by the lack of statistical significance for all random slope terms. This suggests that beyond the household environment, village influences potential exposure to factors that increase diarrhea risk or promote care-seeking and treatment; however, once exposed to such factors, the potential effects are uniform across villages.

Figures 3.2-3.4 illustrate the level of inter-village variation in the village-aggregated outcome measures, though the depicted values are not weighted by the number of included households per village. For all three outcomes, comparison of multilevel logistic regression models 1 and 2, which accounted for the number of households per village through sampling weights, indicated that inter-village variation was still present and was not accounted for by differences in the characteristics of the households comprising each village. This lack of a compositional effect implies that variation in village-specific diarrhea prevalence, care-seeking coverage, and ORS coverage are better explained by village-level determinants than those assessed at the household-level.

At the household-level, the protective effect of access to a toilet or latrine as opposed to open defecation was elevated comparing caregivers from the same village with education beyond primary school education to those with less education (Table 3.3). The role of maternal education and literacy in conferring protection against diarrheal infections among children under-five has been well-documented and is attributable to the improvements in hygiene and sanitation, as well as gains in household socioeconomic status, that are often linked to relative increases in educational attainment [23, 46]. However, it is important to note that educational attainment may not be protective in the absence of improved household-level sanitation; the data showed a trend in increased risk of diarrhea among children from households in which a caregiver was educated beyond primary school but there was no access to a toilet or latrine (Table 3.3).

At the village-level, the proportion of households with toilet/latrine access did not have an effect on the odds of diarrhea (Table 3.3). This finding is unexpected, given the household-level results, and incongruous with existing literature supporting decreased diarrhea risk in communities with improved excreta disposal [20]. This anomaly may be explained by the lack of variability in sanitation practices across villages, since the consistently low proportion of households with toilet/latrine access across all 195 included villages (i.e. village-specific mean: 19.0%; IQR: 3.6-28.0%) could have impeded detection of an effect. Moreover, it is possible that the village-specific proportion of households with toilet/latrine access did not adequately capture true village-level exposure to feces in the environment. The village-specific variable for toilet/latrine access was generated by aggregating observations across included households, which may not have been representative of true sanitation practices among non-included households throughout the village. The models would therefore be improved by village-level data on toilet/latrine access across all households within a given village, since open defecation among neighboring households would impact exposure to feces for the entire community.

A key goal of this study was to assess the extent to which context played a role in predicting household-level diarrhea occurrence, care-seeking and ORS treatment. In this study, the contextual effect was a measure of whether household-level outcomes were influenced by village-level determinants after controlling for household-level predictors. There was a statistically significant contextual effect of caregiver education on the occurrence of diarrhea among children during the two-weeks prior to the survey. This contextual effect can best be interpreted by envisioning two distinct households, each with a child 2-59 months of age and a caregiver educated beyond primary school, but situated within villages that differ by 10% in the proportion of caregivers with more than primary school education. In this scenario, the child from the household situated in the village with higher aggregated educational attainment experienced a 7.4% (95% CI: 3.5-8.9%) decrease in the odds of diarrhea in the two-weeks preceding the survey; the effect size is the same in the case of two caregivers with less than primary school education. This finding suggests that children residing in villages with higher levels of collective knowledge among caregivers are at reduced risk of diarrhea, even if they are raised in a household in which the primary caregiver has had less education. It is likely that this effect is mediated by the improvements to sanitation and hygiene associated with increased educational attainment and literacy among mothers [23, 46]. It is also possible that the variable for village-specific education only captured the nuances of diarrhea risk due to its inclusion in a model with a perhaps poorly designed measure of village-specific exposure to environmental feces. Additional multilevel models should be built to investigate the contextual effect of education when controlling for variables that better represent the overall state of village-level sanitation.

There was no evidence supporting a contextual effect of education on care-seeking or ORS treatment. Care-seeking for diarrhea was strongly associated with increased caregiver education at the household-level, but there was no village-level effect (Table 3.4). Similarly, there was a trend toward a positive association between the odds of ORS treatment and household-level caregiver education but no village-level effect

(Table 3.5). Village-level educational attainment was intended as a proxy measure for collective awareness of adequate childhood diarrhea management throughout the community; however, it is possible that the effect of education on care-seeking and ORS use is more siloed, and that there is limited interaction between caregivers with education beyond primary school and those with less or no formal education. Further research is warranted to assess whether specific measures of social support influence care-seeking and ORS at the village-level.

The failure to observe strong effect sizes for the household and village-specific mean wealth index scores may be attributable to the measure of wealth that was employed. The wealth index scores were generated using established methods for assessing wealth with asset ownership data in the absence of information on income or consumption [44]. It is possible that village-aggregated index scores did not accurately reflect community health infrastructure and economic development, which have been established as important predictors of health service use [34, 36]. Furthermore, household-level asset ownership may not have captured factors increasing the likelihood of care-seeking for diarrhea, such as proximity to public- and private-sector resources.

3.4.2 Limitations

This study was limited by the potential for biased reporting among participating caregivers of children 2-59 months of age. Report of diarrhea, care-seeking and ORS treatment may have been influenced by caregiver education, with outcomes more accurately reported by caregivers that attended additional years of school. Recall of outcomes may have also been influenced by episode severity if caregivers were more likely to forget mild or moderate episodes occurring in the two-weeks prior to the survey. The extent to which episode severity, as measured by reported symptoms, impacts recall and reporting of illness, care-seeking and treatment are discussed in Paper 2.

An additional limitation of this study was the lack of village-level data beyond aggregated household-level variables. Aggregating data from the household-level allowed for improved understanding of the sampled population, which was powered to represent households in which a child 2-59 months of age was in residence; however, households with children 2-59 months of age are not necessarily representative of the overall village population in terms of factors increasing risk for diarrhea and/or promoting care-seeking and ORS treatment. This analysis should be undertaken again using data on village amenities, such as infrastructure, roads, schools, and proximity to reliable sources for childhood diarrhea management, such as hospitals and PHCs.

3.4.3 Broader implications and conclusions

The implications of this study are of great significance to childhood diarrhea management programs, which aim to effectively allocate limited resources, and to program evaluations with the goal of producing unbiased estimates of two-week diarrhea prevalence, coverage of care-seeking and coverage of ORS. The results of this study suggest that educational attainment among caregivers of children under-five is influential in determining care-seeking and treatment for childhood diarrheal episodes; therefore, programs should concentrate promotion of adequate diarrhea management and treatment on households with less educated caregivers and in communities in which collective educational attainment is lower.

In addition, this study highlighted the potential for factors beyond the household to influence outcomes relevant to the success of diarrhea management programs. Programs evaluators should account for inter-village variation in key outcomes in order to generate more accurate estimates of prevalence and coverage, and evaluations should gauge the contextual influences of population-level sanitation practices, education and wealth when assessing program impact.

Table 3.1

Variables considered for inclusion in multilevel models of diarrhea occurrence, care-seeking and ORS treatment

Variable	Description	Outcomes for which variable was tested for model inclusion *
LEVEL: Household		
Child gender	0=Female; 1=Male	Diarrhea, care-seeking, ORS
Child age	Continuous (months)	Diarrhea, care-seeking, ORS
Caregiver age	Continuous (years)	Diarrhea, care-seeking, ORS
Caregiver education	Continuous (years of schooling)	Diarrhea, care-seeking, ORS
Caregiver education	0= Less than primary school (≤7 years); 1= Beyond primary school (>7 years)	Diarrhea, care-seeking, ORS
Below poverty line [a]	Binary (0=Yes; 1=No)	Diarrhea, care-seeking, ORS
Household wealth Index [b]	Continuous score	Diarrhea, care-seeking, ORS
Household wealth quintile [b]	0=Poorest; 1=Very poor; 2=Poor; 3=Less poor; 4=Least poor	Diarrhea, care-seeking, ORS
Child admitted to hospital in previous 3 months	0= Yes; 1=No	Diarrhea
Family type	0=Joint; 1=Nuclear	Diarrhea
Family size	Total number of persons residing in household	Diarrhea

Table 3.1 continued

Variable	Description	Outcomes for which variable was tested for model inclusion *
LEVEL: Household		
Children under-five	0= >1 child under-five residing in household; 1= Only 1 child under-five residing in household	Diarrhea
Purify drinking water	0=No; 1=Yes	Diarrhea
Time to obtain drinking water	0=Water not on premises; 1=Water on premises	Diarrhea
Place of defecation	0=Open defecation/no facility; 1=Toilet/latrine	Diarrhea
Source of drinking water	0=Public tap/tube or bore well/hand pump/dug well/tanker truck/surface water; 1=Piped into dwelling	Diarrhea
Child recovered from diarrheal episode at time of survey [c]	0=No; 1=Yes	Care-seeking, ORS
Episode duration [d]	Episode length in days [d]	Care-seeking, ORS
Care-seeking	0=Did not seek care outside the home; 1=Sought care outside the home	ORS
Public sector care-seeking [e]	0=Did not seek care or sought care through the private sector; 1=Sought care through the public sector	ORS

Table 3.1 continued

Variable	Description	Outcomes for which variable was tested for model inclusion *
LEVEL: Village		
Aggregated wealth index score	Village-specific mean wealth index score	Diarrhea, care-seeking, ORS
Proportion above poverty line	Village-specific proportion of households above poverty line	Diarrhea, care-seeking, ORS
Aggregated caregiver education	Village-specific mean years of education among caregivers of children under-five	Diarrhea, care-seeking, ORS
Proportion of caregivers beyond primary school education	Village-specific proportion of households in which a caregiver of a child under-five has more than primary school education	Diarrhea, care-seeking, ORS
State	0=Gujarat; 1=UP	Diarrhea, care-seeking, ORS
Proportion toilet/latrine	Village-specific proportion of households with access to a toilet/latrine	Diarrhea

[*] Variables were assessed for inclusion using bivariate analyses and Wald tests.

[a] Below poverty line assessed by possession of BPL card.

[b] Wealth quintiles and indexes generated using PCA analysis of asset variables [44].

[c] Children were considered recovered from the index diarrheal episode if they had not passed a loose/watery stool in the 3 days preceding the survey.

[d] For children recovered from diarrhea at the time of the survey, episode duration was the number of days between the reported dates of onset and recovery. For children with a current episode, duration was the number of days between onset and the survey.

[e] Public sector sources of care-seeking included: primary health centers, auxiliary nurse midwives, Anganwadi workers (AWW), and accredited social health activists (ASHA).

Table 3.2

Characteristics of included households and children 2-59 months of age

	All included households N=8085 n (%)	**Households in which child had diarrhea in the two-weeks prior to survey** N=1245 n (%)
Diarrhea in the two-weeks preceding the survey	1245 (15.4)	1245 (100)
Female	3742 (46.3)	606 (48.7)
Child age (months)		
Mean (SD)	24.5 (15.9)	17.7 (13.2)
2-11 months	2136 (26.4)	510 (41.0)
12-23 months	2110 (26.1)	391 (31.4)
24-35 months	1605 (19.9)	189 (15.2)
36-47 months	1237 (15.3)	105 (8.4)
48-59 months	997 (12.3)	50 (4.0)
Joint family [a]	4394 (54.4)	691 (2.8)
Family size (# persons)		
Mean (SD)	6.7 (2.7)	6.9 (2.8)
>1 child under-five in household [b]	3077 (38.1)	623 (50.0)
Caregiver age (years)		
Mean (SD)	27.8 (5.7)	27.2 (5.3)
Caregiver education		
Mean (SD) (years)	3.4 (4.4)	3.1 (4.2)
≤7 years [c]	6258 (77.4)	1003 (80.6)

Table 3.2 continued

	All included households	Households in which child had diarrhea in the two-weeks prior to survey
Below poverty line [d]	2773 (34.3)	452 (36.3)
Wealth quintile [e]		
Least poor	1615 (20.0)	204 (16.4)
Less poor	1618 (20.0)	261 (21.0)
Poor	1617 (20.0)	275 (22.1)
Very poor	1618 (20.0)	266 (21.4)
Poorest	1617 (20.0)	239 (19.2)
State		
Gujarat	3885 (48.0)	594 (47.7)
Uttar Pradesh	4200 (52.0)	651 (52.3)
Hospital admission 3 months prior to survey	144 (1.8)	54 (4.3)
Does not purify drinking water	4577 (56.6)	767 (61.6)
Water not on household premises	3911 (48.4)	612 (49.2)
Open defecation [f]	6474 (80.1)	1041 (83.6)
Drinking water from public tap/ tube or bore well/ hand pump/ dug well/ tanker truck/ surface water [g]	6396 (79.1)	1029 (82.7)
Care sought outside the home for diarrheal episode	-	970 (77.9)
Care sought through the public sector [h]	-	103 (8.8)

Table 3.2 continued

	All included households	Households in which child had diarrhea in the two-weeks prior to survey
Child recovered from diarrheal episode at time of survey [i]	-	507 (40.7)
Episode duration [j]	-	
Mean (SD)	-	4.7 (4.1)
ORS used to treat diarrheal episode	-	232 (18.6)

[a] Remaining 45.6% were nuclear families.

[b] Remaining 61.9% were households with one child <5 years of age (i.e. the child included in the survey).

[c] >7 years of schooling indicates more than primary school education.

[d] Below poverty line assessed by possession of BPL card.

[e] Wealth quintiles and indexes generated using PCA analysis of asset variables following previously published methods [44].

[f] Remaining 19.9% had access to a toilet or latrine.

[g] Remaining 20.9% had piped water into household dwelling.

[h] Public sector sources of care-seeking included: primary health centers, auxiliary nurse midwives, Anganwadi workers (AWW), and accredited social health activists (ASHA).

[i] Children were considered recovered from the index diarrheal episode if they had not passed a loose/watery stool in the 3 days preceding the survey.

[j] For children recovered from diarrhea at the time of the survey, episode duration was defined as the number of days between the reported dates of onset and recovery. For children with a current episode at the time of the survey, duration was calculated as the number of days between reported onset and the survey date.

Table 3.3

Multilevel logistic regression models of the log odds of diarrhea among children 2-59 months of age in the two-weeks preceding the survey ^

Covariate	Model 1: Random intercept for village	Model 2: Random intercept for village + household-level covariates	Model 3: Random intercept for village + household-level and village-level covariates
Intercept (95% CI)^^	0.15 (0.13-0.18)*	1.22 (0.68-2.19)	1.50 (0.75-3.01)
Random intercept variance	0.70 (0.41-0.99)*	0.68 (0.40-0.96)*	0.64 (0.37-0.91)*
		aOR (95% CI)	**aOR (95% CI)**
Child age in months	-	0.97 (0.96-0.97)*	0.97 (0.96-0.97)*
Hospital admission 3 months prior to survey			
No	-	0.28 (0.15-0.52)*	0.28 (0.15-0.52)*
Yes	-	1.0	1.0
Toilet/latrine access [a]			
Caregiver education beyond primary school	-	0.40 (0.15-1.03)	0.40 (0.15-1.05)
Caregiver education ≤ primary school	-	0.79 (0.44-1.44)	0.79 (0.43-1.45)
Household wealth index	-	0.99 (0.95-1.04)	0.99 (0.95-1.04)
Caregiver education (beyond primary school) [a]			
Toilet/latrine access	-	0.65 (0.42-1.00)	0.65 (0.42-1.01)
No toilet/latrine access	-	1.29 (0.94-1.76)	1.28 (0.94-1.76)

Table 3.3 continued

Covariate	Model 1: Random intercept for village	Model 2: Random intercept for village + household-level covariates	Model 3: Random intercept for village + household-level and village-level covariates
Village-specific mean wealth index score	-	-	0.98 (0.84-1.14)
Village-specific proportion of households in which a caregiver of a child under-five has more than primary school education	-	-	0.34 (0.14-0.82)*
Village-specific proportion of households with access to a toilet/latrine	-	-	1.22 (0.40-3.68)

^ Multilevel logistic regression models of the log odds of diarrhea in the two-weeks preceding the survey were fitted in Stata 12.0 using adaptive Gaussian quadrature and 12 integration points and adjusting for the sampling weights of households and villages [43].

^^The intercept is interpreted as the odds of diarrhea (95% CI) when all included covariates equal zero.

*Statistically significant at $p<0.05$

[a] There was a statistically significant interaction between caregiver education and toilet/latrine access.

Table 3.4

Multilevel logistic regression models of the log odds of care-seeking among children with diarrhea in the two-weeks preceding the survey ^

Covariate	Model 1: Random intercept for village	Model 2: Random intercept for village + household-level covariates	Model 3: Random intercept for village + household-level and village-level covariates
Intercept^^	11.79 (7.12-19.52)*	1.01 (0.54-1.90)	1.14 (0.48-2.69)
Random intercept variance	3.64 (1.79-5.49)*	3.64 (1.95-5.33)*	3.61 (1.93-5.29)*
		aOR (95% CI)	**aOR (95% CI)**
Child age			
2-11 months	-	1.44 (0.87-2.37)	1.44 (0.88-2.37)
12-59 months	-	1.0	1.0
Episode duration			
>3 days	-	2.55 (1.57-4.16)*	2.56 (1.57-4.17)*
≤3 days	-	1.0	1.0
Child recovered at time of survey			
Yes	-	3.58 (2.04-6.26)*	3.58 (2.04-6.29)*
No	-	1.0	1.0
State			
UP	-	8.05 (3.98-16.28)*	8.04 (3.97-16.29)*
Gujarat	-	1.0	1.0
Household wealth index	-	0.86 (0.71-1.04)	0.86 (0.72-1.05)
Caregiver education			
> primary school	-	4.08 (1.19-13.92)*	4.10 (1.20-13.98)*
≤ primary school	-	1.0	1.0

Table 3.4 continued

Covariate	Model 1: Random intercept for village	Model 2: Random intercept for village + household-level covariates	Model 3: Random intercept for village + household-level and village-level covariates
Village-specific mean wealth index score	-	-	1.17 (0.86-1.60)
Village-specific proportion of households in which a caregiver of a child under-five has more than primary school education	-	-	0.60 (0.04-9.64)

^ Multilevel logistic regression models of the log odds of diarrhea in the two-weeks preceding the survey were fitted in Stata 12.0 using adaptive Gaussian quadrature and 12 integration points and adjusting for the sampling weights of households and villages [43].

^^The intercept is interpreted as the odds of care-seeking for diarrhea (95% CI) when all included covariates equal zero.

*Statistically significant at $p<0.05$

Table 3.5

Multilevel logistic regression models of the log odds of ORS treatment among children with diarrhea in the two-weeks preceding the survey^

Covariate	Model 1: Random intercept for village	Model 2: Random intercept for village + household-level covariates	Model 3: Random intercept for village + household-level and village-level covariates
Intercept (95% CI)^^	0.15 (0.10-0.22)*	0.002 (0.0003-0.02)*	0.002 (0.0002-0.01)*
Random intercept variance	2.78 (1.37-4.19)*	5.56 (2.20-8.92)*	5.48 (2.17-8.79)*
		aOR (95% CI)	**aOR (95% CI)**
Child age			
2-35 months	-	1.69 (0.64-4.49)	1.69 (0.64-4.49)
36-59 months	-	1.0	1.0
Episode duration			
>3 days	-	1.86 (1.01-3.46)*	1.86 (1.02-3.46)*
≤3 days	-	1.0	1.0
Care sought outside the home			
Yes	-	23.70 (7.15-78.52)*	23.74 (7.16-78.78)*
No	-	1.0	1.0
Any care sought through public sector [a, b]			
Gujarat	-	13.45 (2.93-61.78)*	13.45 (2.93-61.73)*
UP	-	1.79 (0.58-5.57)	1.80 (0.58-5.59)
State (Gujarat vs UP)[a]			
Any care sought via public sector [b]	-	4.90 (0.77-31.28)	4.87 (0.76-31.09)
No care sought via public sector [b]	-	0.65 (0.28-1.49)	0.65 (0.28-1.49)

Table 3.5 continued

Covariate	Model 1: Random intercept for village	Model 2: Random intercept for village + household-level covariates	Model 3: Random intercept for village + household-level and village-level covariates
Household wealth index	-	1.22 (1.02-1.46)*	1.22 (1.02-1.46)*
Caregiver education			
> Primary school	-	1.73 (0.53-5.62)	1.73 (0.53-5.61)
≤ Primary school	-	1.0	1.0
Village-specific mean wealth index score	-	-	1.07 (0.76-1.52)
Village-specific proportion of households in which a caregiver of a child under-five has more than primary school education	-	-	2.23 (0.06-79.92)

^ Multilevel logistic regression models of the log odds of diarrhea in the two-weeks prior to survey were fitted in Stata 12.0 using adaptive Gaussian quadrature and 12 integration points and adjusting for sampling weights of households and villages [43].

^^The intercept is interpreted as the odds of ORS (95% CI) when all included covariates equal zero.

*Statistically significant at $p<0.05$

[a] There was a statistically significant interaction between state and public sector care-seeking.

[b] Reference category for any public sector care-seeking is no public sector care-seeking (i.e. only private sector care-seeking or no care-seeking).

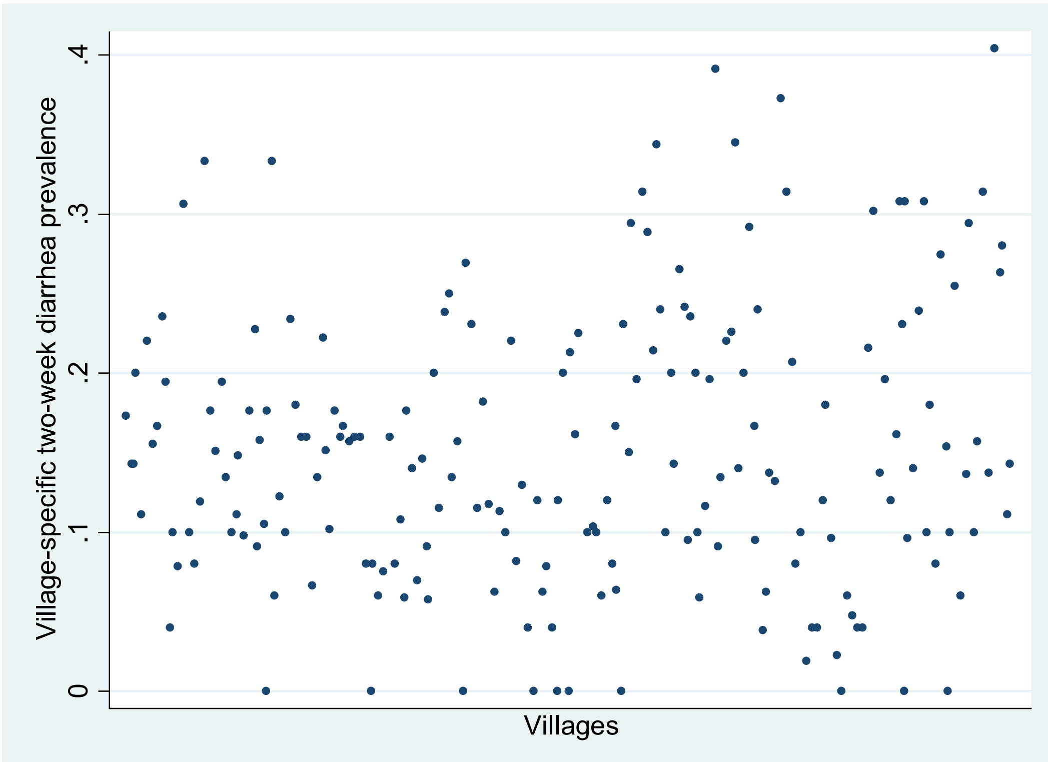
Figure 3.1

DAZT project districts included in baseline phase of the evaluation

Source: Map was generated using ArcGIS software and DIVA-GIS shapefiles [47, 48]. Baseline data collection conducted in 12 districts in UP (*Ambedkar Nagar, Badaun, Bara Banki, Bareilly, Faizabad, Hardoi, Kanpur Dehat, Lucknow, Shahjahanpur, Sitapur, Sultanpur, Unnao*) and 6 districts in Gujarat (*Banas Kantha, Dohad, Panch Mahals, Patan, Sabar Kantha, Surendranagar*).

Figure 3.2

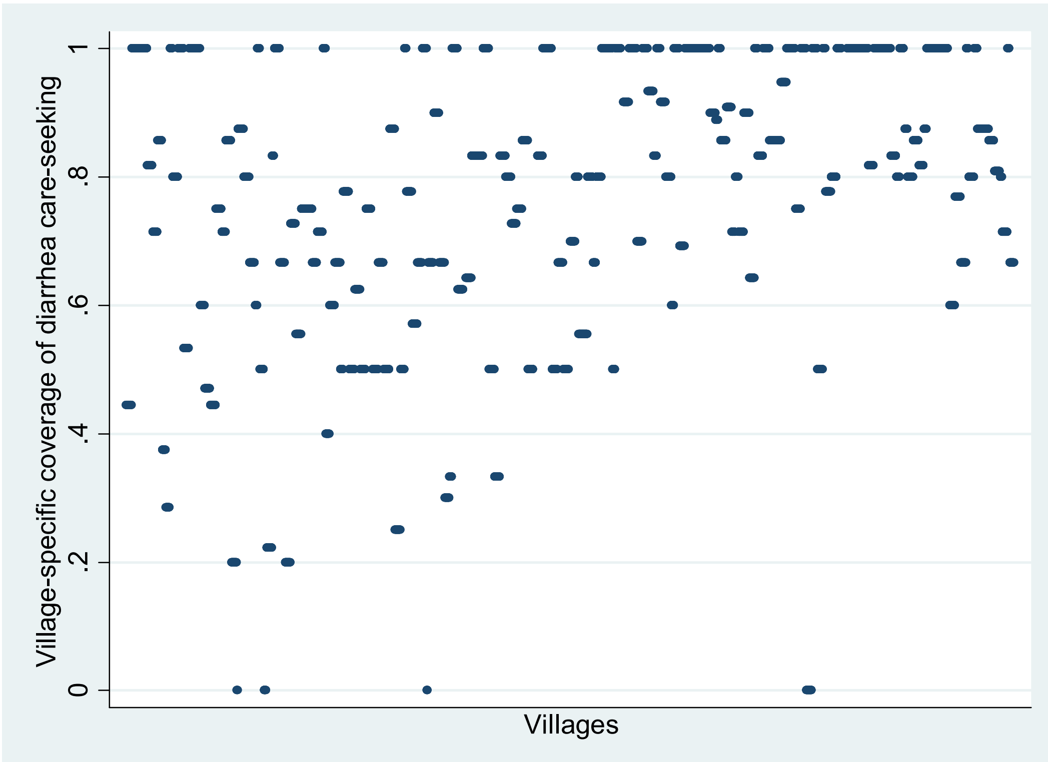
Variation in two-week diarrhea prevalence among children under-five across 195 villages*



* Villages placed at random along horizontal axis; y-axis represents two-week diarrhea prevalence. Values are unweighted and thus influenced by the number of households surveyed per village; multilevel logistic regression analyses are adjusted for sampling weights.

Figure 3.3

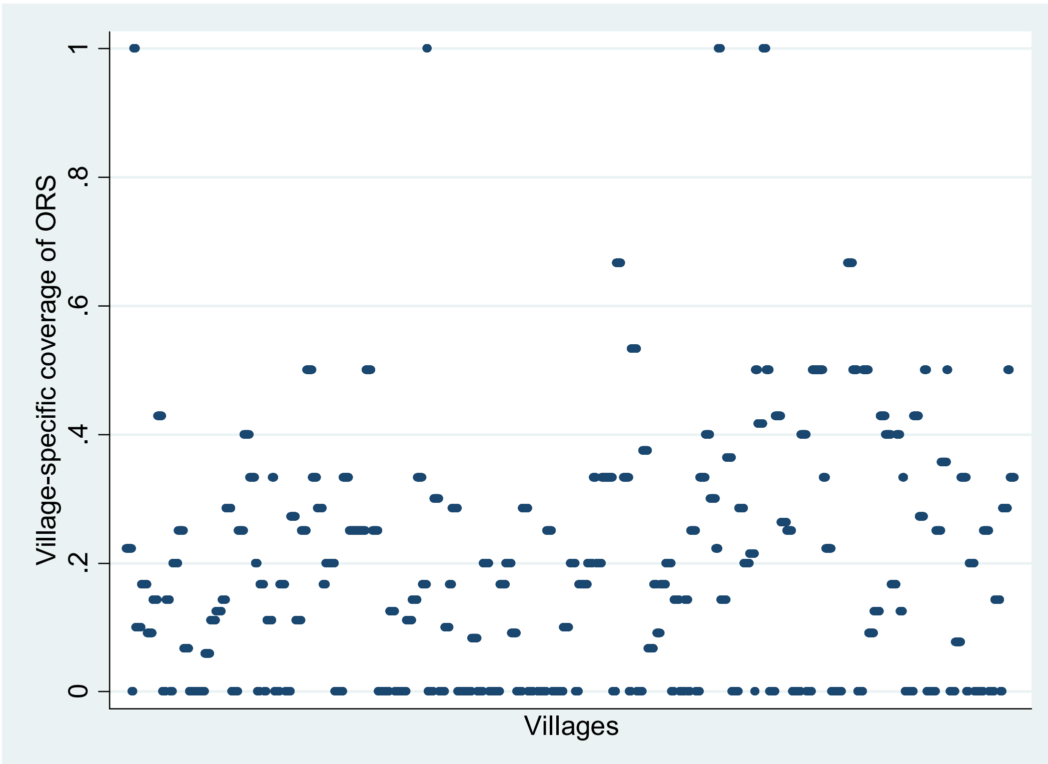
Variation in coverage of care-seeking for diarrhea in a child under-five across 185 villages*



* Villages placed at random along horizontal axis; y-axis represents coverage of care-seeking for diarrhea. Values are unweighted and thus influenced by the number of households surveyed per village; multilevel logistic regression analyses are adjusted for sampling weights.

Figure 3.4

Variation in coverage of ORS treatment for diarrhea in a child under-five across 185 villages*



* Villages placed at random along horizontal axis; y-axis represents ORS coverage. Values are unweighted and thus influenced by the number of households surveyed per village; multilevel logistic regression analyses are adjusted for sampling weights.

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Chapter Four: Paper 2

The influence of episode severity on caregiver recall, care-seeking and treatment of diarrhea among children 2-59 months of age in Bihar, Gujarat and Uttar Pradesh, India

4.1 Introduction

4.1.1 Burden, care-seeking and treatment of diarrhea among children under-five in Bihar, Gujarat and Uttar Pradesh, India

Diarrhea causes high morbidity and mortality among children under-five across India, especially in states with large populations living in rural, impoverished settings [1, 2]. Specifically, the states of Bihar and Uttar Pradesh (UP) rank highest in the country in terms of the crude number of annual diarrheal deaths among children under-five [2, 3]. In comparison, the state of Gujarat has higher GDP per capita and lower under-five mortality [2, 4], but the burden of childhood diarrhea is still significant [2]. Of the approximately 257,000 diarrheal deaths among children under-five in 2007, an estimated 28,959, 11,960 and 69,451 occurred in Bihar, Gujarat and UP, respectively [2]. Furthermore, in 2005-2006, two-week prevalence of diarrhea among children under five years of age was 9% nationally, 13% in Gujarat, 11% in Bihar and 8% in UP [5-8].

In accordance with global recommendations by WHO/UNICEF [9], the Government of India and the Indian Academy of Pediatrics endorse the treatment of under-five diarrheal episodes with reduced osmolarity oral rehydration salts solution (ORS) and 10-14 days of supplementation with 20 mg of zinc/day for children ≥ 6 months and 10 mg of zinc/day for infants <6 months [10, 11]. Reduced osmolarity ORS has been shown to treat and prevent dehydration and death due to diarrhea [12]. When administered in addition to ORS, therapeutic zinc supplementation reduces the duration, severity and recurrence of diarrhea among children under five years of age [13].

Despite national guidelines for the management of childhood diarrhea, care-seeking and coverage of ORS and therapeutic zinc are low throughout India. From 2005-2006, health facility care was sought for approximately 60% of diarrheal episodes among Indian children under five years of age [8], and in Bihar, Gujarat and UP, this figure was 54%, 57% and 58%, respectively [5-7]. During the same period, ORS coverage was 26% across India, 21% in Bihar, 26% in Gujarat and 13% in UP; zinc coverage had yet to be scaled-up nationally and was consequently ≤0.5% in these three states [8].

4.1.2 Measuring the occurrence of diarrhea among children under-five

The occurrence of childhood diarrhea can be measured through various study designs. Cohort studies collect longitudinal data on a sample of children during a defined period of observation, which allows for the calculation of diarrhea incidence (e.g. *cumulative incidence* defined as the proportion of observed children that experience at least one episode of diarrhea during the observation period, and *incidence density* defined as the total number of diarrheal episodes divided by total person-time at risk) [14]. However, due to the time-consuming and expensive nature of cohort studies, cross-sectional studies are more commonly utilized to assess the point or period prevalence of childhood diarrhea in large populations [14]. Cross-sectional surveys designed to assess maternal and child health outcomes typically include a question on the occurrence of diarrhea among children under-five during the 24-hours and the two-week time periods preceding the survey, and these data are utilized to calculate the point prevalence and the two-week period prevalence of under-five diarrhea in a given population [8, 15]. In India, the International Institute for Population Sciences (IIPS) routinely administers a large-scale cross-sectional household survey, known as the National Family Health Survey (NFHS), to representative samples in each state in order to assess the two-week prevalence of diarrhea among children under-five, as well as other maternal and child health indicators [16].

4.1.3 Measuring the severity of diarrhea among children under-five

In the literature, various outcomes are utilized as measures of diarrheal severity among children under-five years of age [17]. In clinical settings and in studies with active surveillance, the Hjelt and Vesikari scales can be used to gauge the degree of episode severity by assigning points based on the level of seriousness of several symptoms: episode duration, vomiting duration, maximum stool frequency, maximum temperature and maximum percent dehydration [18, 19]. The assessment of these symptoms necessitates daily monitoring by trained health workers with adequate medical instrumentation, including stool collection vials, rectal thermometers, and scales to measure acute weight loss for calculation of percent dehydration.

Consequently, studies designed to collect data on childhood diarrhea in the community are usually not equipped to adequately assess episode severity. As an alternative approach, surveys often collect caregiver-reported data on episode duration, stool frequency (i.e. maximum number of stools/day), and the presence of fever and vomiting. Given the difficulty of assessing dehydration in the community and the unfamiliarity of caregivers with the term, surveys also collect data on the presence of symptoms associated with dehydration, such as reduced skin turgor, lethargy, irritability and sunken eyes.

4.1.4 The threat of recall bias in measuring the occurrence of diarrhea among children under-five using cross-sectional surveys

Cross-sectional household surveys rely heavily on the recall of primary caregivers (typically mothers) to accurately report the occurrence and characteristics of their children's diarrhea during a specified interval of time. Assuming that diarrhea is equally likely to occur at any point during a short time period (i.e. during the same diarrhea season), the number of episodes reported on each day within a recall interval should be comparable [20, 21]. However, caregivers may fail to remember illness that occurred earlier in the recall period, and such recall errors can bias estimates of disease occurrence [20-24].

While two-week recall of diarrhea is widely accepted, studies have suggested that errors in recall increase over the course of a 1-2-week interval and, therefore, shorter recall periods are optimal [20-24]. A study in Kenya reported an increase in diarrhea incidence comparing recalled episodes with onset 0-6 versus 7-13 days before home visits (RR: 2.39; 95% CI: 2.20-2.59) and a ≥20% decrease in diarrhea prevalence comparing episodes recalled ≥3 days before the visit to those recalled on days 0-2 [22]. A study in Guatemala found that when comparing the proportion of recalled episodes with onset dates 1-2 days before the survey to those with onset dates 3-6 days before the survey, recall error increased from 37% on day 3 to 48% on day 6 [20]. Using multi-country data, Arnold et al. concluded that a 7-day recall period for under-five diarrheal episodes was optimal because further shortening the recall period improved accuracy but resulted in increased sample size requirements that were not logistically feasible [23].

4.1.5 The potential influence of diarrheal severity on recall

According to the 'Salient Principle,' the accuracy of illness reporting is higher when symptoms are more severe [22, 25, 26]. In support of this principle, there is evidence that recall errors are less likely to occur for severe diarrheal episodes among children under-five [20, 21]. A study in Bangladesh concluded that recall errors were inversely related to stool frequency and that diarrheal episodes accompanied by vomiting were reported more accurately [21]. A Guatemalan study found that when 'severe' was defined as a maximum stool frequency of >5 stools in a 24-hour period, the odds of a severe episode were higher among those with onset dates 3-6 days prior to the interview compared to those with onset dates 1-2 days prior to the interview (OR: 2.1; 95% CI: 1.81-2.42) [20]. These findings suggest that in addition to underestimating the occurrence of diarrhea among children under-five, longer recall periods disproportionately capture more severe episodes [20].

Still, the 'Salient Principle' has not been supported by other studies that utilized alternate definitions for severe diarrhea among children under-five [22, 27]. A Kenyan-based study, which defined severe diarrheal episodes for children under-five as those that included a diarrhea danger sign or met the WHO severe dehydration criteria from the Integrated Management of Childhood Illnesses (IMCI) algorithm [28], found that the relative risks of diarrhea occurring 0-6 versus 7-13 days before the household interview were equivalent comparing severe to non-severe episodes (RRR: 0.98; 95% CI: 0.89-

1.07) [22]. A study conducted on infants in the Gambia found that, like diarrhea, the prevalence of fever and vomiting were inversely related to the length of the recall period, suggesting that diarrhea accompanied by fever or vomiting is not more memorable than less severe episodes without these additional symptoms [27].

Research is therefore warranted to establish the influence of diarrheal severity on caregiver recall in different geo-cultural contexts and utilizing varying definitions for what constitutes a severe episode. It is possible that accurate recall is less dependent on actual severity than on caregivers' perceptions that certain characteristics of diarrheal episodes indicate severity. For example, in the Guatemala study, episodes accompanied by the presence of blood in stools were associated with less frequent errors in recall and with higher odds of occurrence among those with onset dates 3-6 days versus 1-2 days prior to the interview (OR: 1.5; 95% CI: 1.08-2.12) [20]; although bloody stools signify that a child has dysentery and not necessarily that the episode is more severe than one without bloody stools, caregivers may have the impression that this characteristic is serious and therefore worth remembering. A study assessing caregivers' perceptions of various diarrheal episode characteristics was conducted in Kolkata, India and reported that caregivers perceived diarrhea accompanied by bloody stools (93.6%), vomiting (95%) and dehydration (83.1%) to be indicative of severe diarrhea [29]. Further research is therefore important to establish whether caregiver recall of diarrhea among children under-five is impacted by various episode characteristics in Bihar, Gujarat and UP, India.

4.1.5 The potential influence of diarrheal severity on care-seeking and treatment

In addition to influencing recall, perceptions about the severity of a diarrheal episode may impact a caregiver's decision to seek care outside the home and to purchase and/or administer certain treatments [29-31]. Studies in Yemen and Kolkata, India have reported an association between perceived episode severity and care-seeking for diarrheal illness [29, 31]. A multi-country study found that in India, children for which diarrhea care and treatment were sought at a health facility experienced higher odds of fever (aOR: 3.9; 95% CI: 1.19-12.85); however, there was no association between care-seeking and other signs of severe diarrhea [32]. A recent study utilized NFHS data from 2005-2006 to assess differentials in diarrhea care-seeking and treatment in India but noted lack of data on episode severity as a major limitation of the analysis [33]. Research is therefore necessary to establish whether the presence of certain episode characteristics affects care-seeking and ORS/zinc treatment practices for diarrhea among children under-five years of age in Bihar, Gujarat and UP, India.

4.1.6 Nesting of research questions within an evaluation of diarrhea management programs in Bihar, Gujarat and Uttar Pradesh, India

This study sought to assess the influence of diarrheal episode severity on caregiver recall, care-seeking and ORS/zinc treatment for diarrhea among children under-five. These research questions were addressed using data collected for the primary purpose of a large-scale evaluation of the Diarrhea Alleviation through Zinc and ORS Treatment (DAZT) program in Gujarat and UP and a similar scale-up program in Bihar. Funding for the DAZT and Bihar programs were made available by the Bill and Melinda

Gates Foundation (BMGF) and the Children's Investment Fund Foundation (CIFF), respectively, starting in the fall of 2010. Scale-up activities were implemented by Micronutrient Initiative (MI) in the public sectors of all three states and by FHI 360 in the private sectors of Gujarat and UP. The Johns Hopkins University Institute for International Programs (JHU IIP) and the Society for Applied Studies (SAS) in New Delhi were responsible for evaluating both programs.

4.2 Methods

4.2.1 Sample Size Requirements for the Overarching Evaluation

Cross-sectional household surveys were conducted during the baseline and midline phases of the diarrhea management program evaluation. Table 4.1 details the calculations of the sample sizes required at the baseline and midline phases of the evaluation. ORS rather than zinc coverage was used as the basis for sample size calculations because, prior to project implementation, zinc had yet to be scaled-up in the project districts and zinc coverage was therefore very low. Baseline sample size requirements were calculated at the state-level for a precision estimate of the proportion of children 2-59 months of age that received ORS to treat an episode of diarrhea occurring in the two weeks prior to the survey. Midline sample size requirements were calculated to estimate the difference in this proportion from that measured at baseline in UP and Gujarat; midline data were not collected in Bihar due to CIFF budget constraints. The sample size of caregivers of children 2-59 months of age that was required for baseline data collection was 2,409 in Bihar, 4,167 in Gujarat and 3,889 in UP. The sample sizes required at midline were 911 in Gujarat and 1,522 in UP.

4.2.2 Sampling Design

Baseline data collection took place in all project districts, including 15 in Bihar, 12 in UP and 6 in Gujarat (Figure 4.1). At midline, data collection was restricted to the 8 districts in UP and 4 districts in Gujarat where the program had been implemented according to schedule, such that program-attributable changes from baseline could be realistically measured by a midline survey (Figure 4.1).

A systematic sampling design was employed to randomly select caregivers of children 2-59 months of age from villages within included project districts (Figure 4.1). For a given state, the required sample size was divided equally across the included districts. For each district, a list of villages was generated from 2001 government census data [34], and the villages were randomly rank-ordered using Stata 10.0 [35]. Trained data collection teams visited the villages within a district in rank order until the district-required sample size was achieved.

In each village, the data collection team coordinator divided the area into four geographic quadrants. Data collectors were split between the quadrants and began visiting households from a randomly selected location within their assigned quadrant using the right hand rule (i.e. they stood at a central location within the quadrant and began visiting households to the right of that location). In a given village, data collection continued until either all households within the village were visited or the survey was administered to a maximum of 50 caregivers of children 2-59 months of age.

4.2.3 Interviewer Training

All interviewers received comprehensive training in New Delhi prior to implementation of baseline and midline data collection. Training was comprised of instructional sessions, as well as mock interviews and form filling. In addition, training included lessons on the logistics of field operations. While stationed in the field, data collection supervisors periodically conducted refresher sessions to reiterate the training received in New Delhi.

4.2.4 Ethical Approval

Ethical approvals for all phases of this study were obtained from the Johns Hopkins University Institutional Review Board (IRB) in Baltimore, MD and from the Society for Applied Studies Ethical Review Committee (ERC) in New Delhi, India. Interviewers obtained informed consent from all caregivers of children 2-59 months of age that participated in the study. Consent forms were written in English, translated into the local language (i.e. Hindi in Bihar and UP and Gujarati in Gujarat) and then back-translated into English to ensure accuracy. Participants provided their signatures to indicate consent to participate in the study; in lieu of a signature, illiterate participants provided their thumbprints alongside the signature of a literate witness.

4.2.5 Data Collection

Baseline data were collected from March-June 2011, and midline data were collected from September-October 2012. Data collectors screened households for residing children 2-59 months of age with caregivers readily available for participation in the survey. Eligible participants resided in the study area and were the designated caregiver of at least one child 2-59 months of age. A caregiver was defined as the principal individual in charge of looking after a child; in most cases the mother held this role, but the grandmother operated as the primary caregiver in some households due to the death or absence of the mother. In households with multiple children 2-59 months of age, the youngest child was utilized for the basis of survey questions.

Interviewers administered the survey to all consenting caregivers in the local language. The survey consisted of two sections: part one included questions on demographics and diarrhea management knowledge and was completed for all participants; part two contained questions on recent diarrheal morbidity and care-seeking and was only administered to caregivers of children that had experienced diarrhea in the two weeks preceding the survey. The interview lasted about 20 minutes for participants given part one and 30 minutes for participants given parts one and two of the survey.

4.2.6 Quality Control

Coordinators checked forms for accuracy nightly, and inconsistencies were resolved in the field. Data were entered into predesigned databases and cleaned at SAS headquarters in New Delhi. Additional discrepancies identified during data entry were sent to the field for resolution, when possible.

4.2.7 Power Calculations

Across all states and study phases, data were collected from 2,132 caregivers of children under-five that had experienced diarrhea in the two-weeks preceding the survey (i.e. 936 in UP; 759 in Gujarat; and 437 in Bihar). Given the number of interviews achieved, Stata 12.0 was used to calculate the power with which each primary outcome of this analysis could be estimated [36]. For the analysis of the potential influence of diarrheal severity on caregiver recall, the primary outcome was the difference in the proportion of severe cases comparing episodes with reported onset ≥7 days prior to the survey (i.e. more distant onset) to those with reported onset <7 days prior to the survey (i.e. more recent onset). Since severe episodes represent only 0.5% of diarrhea cases among children under-five [17], power was calculated for the difference in the proportion of episodes with any dehydration by distant versus more recent reported onset (Table 4.2). For the analysis of the potential influence of diarrheal severity on care-seeking, the primary outcome was the difference in the proportion of severe and non-severe episodes for which care was sought. Power was calculated for the difference in the proportion of episodes with any dehydration for which care was sought and the proportion of episodes with no dehydration for which care was sought (Table 4.3). For the analysis of the potential influence of diarrheal severity on ORS/zinc treatment, power was calculated for the difference in the proportion of episodes with any dehydration treated with ORS/zinc and the proportion of episodes with no dehydration treated with ORS/zinc (Table 4.4). Tables 4.2-4.4 outline the power achieved for each of the primary outcomes at the alpha=0.05 level under a range of reasonable values for the proportions and minimum detectable differences. These calculations confirmed that power was adequate to carry out these analyses.

4.2.8 Defining indicators of diarrheal severity for data analysis

The responses to survey questions on various characteristics of the diarrheal episode were utilized to define indicators of diarrheal severity. Binary variables were generated to indicate the presence or absence of blood in stools, fever, and vomiting during the episode. The reported maximum number of loose or watery stools passed on any day during the diarrheal illness was used to generate a discrete variable for maximum stool frequency, as well as a binary indicator of whether stool frequency exceeded 5 stools per day.

For episodes that had resolved prior to the time of survey, a discrete variable for the duration of the diarrheal episode in days was generated using the difference between the reported dates of episode recovery and episode onset; for episodes still in progress at the time of the survey, duration was defined as the difference between the date of the survey and the reported date of diarrhea onset. By these definitions, there were four extreme values for diarrheal duration, which were identified by plotting the studentized residuals and Cook's distances; the extreme values were subsequently dropped from the analysis under the assumption that either onset dates were erroneously reported or illness was chronic and therefore not comparable to the other episodes in the dataset. Two binary variables were also generated to indicate whether episode duration exceeded 5 days or 2 days.

Using WHO's IMCI classification criteria for diarrhea-associated dehydration, a binary variable was defined to indicate whether the diarrheal episode was accompanied by 'any dehydration' [28]. According to the IMCI criteria, dehydration is classified as severe when two of the following signs are present: unconsciousness/lethargy, sunken eyes, the inability to drink or drinking poorly, and reduced skin turgor as indicated by skin pinch; whereas, the presence of two of the following signs is indicative of some dehydration: restlessness/irritability, sunken eyes, drinking eagerly or extremely thirsty, and reduced skin turgor [28]. The IMCI classifications were applied to available data in order to generate a measure of 'any dehydration' (i.e. some or severe dehydration).

4.2.9 Data analysis assessing the influence of diarrheal severity on caregiver recall

Data analysis was based on the previously published assumption that diarrheal episodes occur with equal distribution over a given recall interval and that other factors account for the skewed distribution of recalled episodes by onset date, which are generally underreported at >1-2 days prior to data collection [20, 21]. Given a recall interval of 14 days, the analysis was designed to test the hypothesis that recalled diarrheal episodes with more distant onset (e.g. ≥7 days prior to the survey) are more severe than those with more recent onset (e.g. <7 days prior to the survey).

In order to gauge whether episode recall waned over time, recall errors were calculated for the periods 1-7 and 8-14 days prior to the survey. Recall error is a measure of the percentage difference between the number of episodes with reported onset during a given interval and the number that would have been reported if the reporting rate had been consistent with that for episodes with onset 1-2 days prior to the survey [20, 21]. Recall error for the period 1-7 days prior to the survey was calculated by the following formula [20, 21]:

$$100 * \left(\frac{(\text{Reference value}*7)-(\text{Total \# episodes with onset 1}-7\text{ days prior to survey})}{(\text{Reference value}*7)}\right).$$

Reference value refers to the average number of episodes with reported onset 1-2 days prior to the survey (i.e. the total number of episodes with onset 1-2 days prior to the survey divided by 2). The recall error for the period 8-14 days prior to the survey was calculated by substituting the total number of episodes with onset 8-14 days prior to the survey into the numerator of the formula. Episodes occurring on the date of data collection were not included in this calculation because they were not representative of a full day of data collection (n=4).

Logistic regression analyses of the influence of severity on recall were conducted solely using data from children that had recovered from diarrheal illness by the time of the survey; those that had experienced loose or watery stools within 72-hours of the survey were therefore excluded. As a result, the analysis was restricted to children with diarrhea onset dates ≥3 days prior to the survey. Children with diarrhea onset dates occurring >14 days (N=17) before the survey were also excluded from the analysis because it was assumed that recall of exact dates beyond 14 days would be more prone to recall bias. For included children, a binary outcome variable was generated to indicate whether onset of the diarrheal episode had occurred 7-14 days or 3-6 days prior to the survey.

The logistic regression analyses were designed to assess whether the odds of various indicators of diarrheal severity were elevated among diarrheal episodes occurring 7-14 days versus 3-6 days prior to the survey. Bivariate analyses separately modeled the log odds of each severity variable (i.e. any dehydration, blood in stools, vomiting, fever, and maximum stool frequency >5 stools/day) comparing diarrhea onset of 7-14 days to 3-6 days preceding the survey. A multivariable logistic regression model was fitted for the log odds of the outcome (i.e. onset 7-14 days versus 3-6 days prior to the survey), controlling for the other indicators of severity, as well as episode duration, child's age and sex, state, and caregiver's education (>7 years vs. ≤7 years, where 7 years is the duration of primary school in India). The multivariable model was inspected for interaction of severity variables with child age and with episode duration exceeding 2 days, and Wald tests were used to assess the statistical significance of such interactions. All analyses were conducted in Stata 12.0 using the robust cluster estimator of variance with village defined as the cluster variable [36].

4.2.10 Data analysis assessing the influence of diarrheal severity on care-seeking and treatment with ORS and zinc

Data analysis was designed to test the hypothesis that care-seeking and ORS/zinc treatment of diarrhea are higher for episodes with various indicators of severity than for those in which such signs are absent. Survey data were utilized to generate binary outcome variables for whether care was sought outside the home, whether the episode was treated with ORS, and whether the episode was treated with zinc. Using Stata 12.0 [36], multivariable logistic regression analyses were conducted to model the log odds of each of these outcomes as a function of various severity variables (i.e. any dehydration, blood in stools, vomiting, fever, and maximum stool frequency >5 stools/day). These models employed the robust cluster estimator of variance and controlled for episode duration, child's age and sex, state, caregiver's education, and whether the child had recovered from the episode or the episode was ongoing at the time of the survey. In addition, models of ORS and zinc treatment controlled for the sector through which care was sought and for the interaction between state and care-seeking sector, since ORS/zinc products may not have been available through all sectors in every state. All models were inspected for statistically significant interactions between severity variables and child age and episode duration.

For caregivers that sought care outside the home, an additional analysis was conducted with the goal of identifying the severity and demographic variables associated with seeking care through one sector versus another. A categorical outcome variable was generated to indicate whether care was obtained through the public sector alone, the private sector alone, or both sectors. Sources of public sector care-seeking included primary health centers (PHCs), auxiliary nurse midwives (ANMs), Anganwadi workers (AWW) and Accredited Social Health Activists (ASHAs), and sources of private sector care-seeking included private doctors and hospitals, chemists, traditional healers and rural medical practitioners (RMPs). Employing the robust cluster estimator of variance, Stata 12.0 was used to build multinomial logistic regression models for care-seeking channel [36]. Wald tests of statistical significance and the Akaike Information Criterion (AIC) were used to determine whether explanatory variables for severity (i.e. any dehydration, blood in stools, vomiting, fever, episode duration, and maximum stool frequency >5 stools/day) and demographic variables (i.e. child's age and sex, caregiver's education, and state) should be retained in the model [37].

4.3 Results

4.3.1 Demographic and diarrheal characteristics

Table 4.5 outlines the key demographic and diarrheal episode characteristics of children with diarrhea in the two-weeks preceding the survey. A slight majority of included children were male (53.1%). The mean age among participating children was 18.0 (SD: 13.4) months, and 41% of children were between the ages of 2-11 months. Only 19% of caregivers had received more than a primary school education (i.e. >7 years).

Commonly reported characteristics of diarrheal episodes included fever (72.3%), vomiting (43.9%) and maximum stool frequency >5 stools/day (38.5%). Any dehydration (25.4%) and blood in stools (12.2%) were less commonly reported symptoms. On average, maximum stool frequency was approximately 6 stools per day (SD: 2.5). Mean episode duration was approximately 4 days (SD: 3.9), and the percentages of episodes exceeding 2 days and 5 days in duration were 64.5% and 24.0%, respectively. At the time of the survey, less than half of included episodes (44%) met the definition for a resolved episode (i.e. at least 72-hours without passing a loose/watery stool).

4.3.2 The influence of diarrheal severity on caregiver recall of diarrhea

The recall errors for the periods of 1-7 and 8-14 days prior to the survey were 4.8% and 31.2%, respectively. The distribution of all 2,132 recalled diarrheal episodes by reported date of onset was not uniform across the period of time preceding the survey (Figure 4.2). Figure 4.2 depicts a large peak at 2 days, which indicates that reported onset of recalled episodes most commonly occurred 2 days prior to data collection. Following 2 days, the number of recalled episodes declines over time, but there are slight peaks at 7 and 14 days.

Regression analyses were conducted using data on the 917 children that had recovered from diarrhea by the time of the survey and whose episode duration did not exceed 14 days. Due to the definition of a recovered episode (i.e. no passage of loose/watery stools in the 72-hours preceding the survey), reported onset dates ranged from 3-14 days among included children. Of the 917 children included in this analysis, the reported diarrhea onset date occurred 3-6 days prior to the survey for 176 (19.2%) and 7-14 days prior to the survey for 741 (80.8%).

In bivariate analyses, the odds of severe diarrheal characteristics were statistically significantly elevated among children with more distant versus more recent diarrhea onset (Table 4.6). Comparing children with diarrhea onset 7-14 days prior to the survey to those with onset 3-6 days beforehand, the odds of any dehydration, blood in stools, fever, vomiting and maximum stool frequency >5 stools/day were elevated by 1.59 (95% CI: 1.09-2.33), 2.02 (95% CI: 1.11-3.70), 1.72 (95% CI: 1.18-2.50), 1.80 (95% CI: 1.29-2.53) and 2.01 (95% CI: 1.34-2.02), respectively (Table 4.6).

Table 4.7 illustrates a trend towards higher odds of any dehydration (aOR: 1.29; 95% CI: 0.84-1.98), fever (aOR: 1.23; 95% CI: 0.81-1.88), vomiting (aOR: 1.26; 95% CI: 0.87-1.84), and maximum stool frequency >5 stools/day (aOR: 1.07; 95% CI: 0.68-1.68) comparing episodes with onset 7-14 days prior to the survey to those with onset 3-6 days prior to the survey, controlling for episode duration, child's age and sex, caregiver's education and state. There was a statistically significant interaction between the binary variables for blood in stools and episode duration >2 days (p=0.038), such that increased odds of blood in stools were associated with onset of 7-14 versus 3-6 days prior to the survey solely among episodes lasting at least 3 days in duration (aOR: 8.03; 95% CI: 1.08-59.54; Table 4.7). There were no statistically significant interactions between severity variables and child age.

4.3.3 The influence of diarrheal characteristics on care-seeking

Of the 2132 caregivers included in this analysis, the majority (n=1690; 79.3%) reported having sought care outside the home for their child's diarrheal episode (Table 4.5). Care was predominantly sought through the private sector alone (87.2%) as compared to the public sector alone (5.8%) or to both sectors (3.7%) (Table 4.5). Figure 4.3 illustrates that the proportion of caregivers that sought care far exceeds the proportion that did not seek care for episodes with any dehydration, blood in stool, fever, vomiting, maximum stool frequency>5 stools/day, and duration >2 days.

The odds of care-seeking were elevated among children with any dehydration (aOR: 1.68; 95 CI: 1.19-2.36), blood in stools (aOR: 1.26; 95% CI: 0.84-1.88), fever (aOR: 2.31; 95% CI: 1.79-3.00), vomiting (aOR: 1.85; 95% CI: 1.41-2.43), maximum stool frequency >5 stools/day (aOR: 1.79; 95% CI: 1.33-2.42), and increased episode duration (aOR: 1.09; 95% CI: 1.03-1.15), controlling for child's age and sex, caregiver's education, state, and whether the child had already recovered from the episode at the time of the survey (Table 4.8). There were no statistically significant interactions between child age and any of the severity variables.

There was no association between the channel through which care was sought and report of fever, vomiting or blood in stools, so these variables were removed from the multinomial logistic regression model. The relative risk of seeking care through the private sector alone versus the public sector alone was 1.78 (95% CI: 1.02-3.13) times higher among children with any dehydration, controlling for episode duration, child's age and sex, caregiver's education, state and whether the child had recovered from diarrheal illness by the time of the survey (Table 4.9). In addition, the relative risk of seeking care through both sectors as compared to the private sector alone increased by 15% (95% CI: 6-25%) per 1 stool/day increase in maximum stool frequency, controlling for other variables (Table 4.9). The relative risk of public versus private sector care-seeking was elevated by a factor of: 6.62 (95% CI: 3.72-11.80) in Gujarat compared to UP, 1.37 (95% CI: 0.63-2.97) in Bihar compared to UP, and 4.85 (95% CI: 2.38-9.86) in Gujarat compared to Bihar (Table 4.9).

4.3.4 The influence of diarrheal severity on treatment

Treatment of diarrheal episodes with ORS (18.4%) and zinc (3.8%) was not commonly reported among caregivers (Table 4.5). The adjusted odds of ORS treatment were elevated among children with vomiting (aOR: 1.85; 95% CI: 1.43-2.39) and maximum stool frequency >5 stools/day (aOR: 1.53; 95% CI: 1.20-1.95) (Table 4.10). There was a statistically significant interaction between the binary variable for any dehydration and the continuous variable for child age centered at 2 months; the adjusted relative odds of ORS treatment comparing dehydrated to non-dehydrated children 2 months of age was 1.60 (95% CI: 1.10-2.34), and this OR decreased by 2.1% (95% CI: 0.5-3.7%) per one month increase in age, holding all other variables constant (Table 4.10).

The analysis also controlled for the interaction of state and the sector through which care was sought; the adjusted odds of receiving ORS treatment if care was sought through the public sector at all (i.e. the public sector alone or both the public and private sectors) compared to the private sector alone were 4.73 (95% CI: 2.86-7.84) in Gujarat, 4.40 (95% CI: 1.77-10.93) in Bihar, and 1.22 (95% CI: 0.55-2.69) in UP (Table 4.10). Additionally, caregiver education beyond primary school (i.e. >7 years) was associated with higher odds of ORS treatment (aOR: 1.35; 95% CI: 1.02-1.80) (Table 4.10).

Maximum stool frequency >5 stools/day (aOR: 1.71; 95% CI: 1.05-2.79) and episode duration >2 days (aOR: 1.12; 95% CI: 0.68-1.83) were the only diarrheal characteristics associated with higher odds of zinc treatment (Table 4.11). The adjusted odds of zinc treatment were also elevated among males (aOR: 1.55; 95% CI: 0.97-2.46) and children of caregivers with education >7 years (aOR: 1.19; 95% CI: 0.67-2.12; Table 4.11). The effect of the sector through which care was sought on zinc treatment was modified by state; the adjusted OR comparing any public sector care-seeking to private sector care-seeking alone was 8.85 (95% CI: 3.32-23.57) in Gujarat, 20.3 (95% CI: 5.60-73.58) in Bihar, and 2.12 (95% CI: 0.60-7.52) in UP (Table 4.11).

4.4 Discussion

4.4.1 General findings

The results of this study demonstrate the potential influence of various diarrheal episode characteristics on the recall, care-seeking and treatment of diarrhea among children under-five.

As evidenced by the distribution of diarrheal episodes by date of onset (Figure 4.2), caregiver recall of diarrhea among children under-five wanes over time; in the absence of recall decay, this distribution would appear uniform because diarrhea is assumed to occur with relatively equal prevalence over short intervals of time. Heaping of reported onset at days 7 and 14 suggests that there was a tendency to report episode onset to the nearest week and as a result, episodes starting mid-week are likely displaced on the graph. Still, the comparison of the recall error for the period 1-7 days prior to the survey (i.e. 4.8%) to that 8-14 days beforehand (i.e. 31.2%) indicates substantial recall decay over time.

While recalled diarrheal episodes were reportedly less common on days more distant from the survey date, the odds of any dehydration, fever, vomiting and maximum stool frequency >5 stools/day were elevated among children with more distant as opposed to more recent illness onset (Table 4.7). This finding suggests that although caregivers forget past episodes of diarrhea as time goes by, the presence of various symptoms increases the likelihood that a more distant diarrheal episode will be remembered and reported. Further research is warranted to determine whether caregivers better recall diarrheal episodes paired with these symptoms because they are considered indicative of increased diarrheal episode severity or because the symptoms themselves are more memorable.

There was a strong correlation between diarrhea care-seeking and the presence of any dehydration, fever, vomiting, and maximum stool frequency >5 stools/day (Table 4.8). In addition, any dehydration and vomiting were linked to receipt of ORS (Table 4.9), and increased stool frequency was associated with both ORS and zinc treatment

(Tables 4.9-4.10). These results imply that perceived episode severity influences caregivers' decision to seek care outside the home and to obtain or purchase treatment. However, it is also possible that care-seekers are more likely than those not seeking care to recall and report various episode characteristics because the act of pursuing care outside the home makes the details of the episode more memorable. Likewise, caregivers of children that received treatment for the diarrheal episode may have better recall of specific symptoms than caregivers of untreated children.

4.4.2 Study limitations

An important limitation of this study is that it was solely conducted from an etic approach and did not account for local perceptions and understanding of diarrheal illness in young children. It is possible that recall, care-seeking and treatment were motivated by symptoms falling into locally recognized categories but because of mismatch with medical terminology, they were excluded from the analysis. A study conducted in Thailand, which undertook an emic approach to assess the practical implications of cultural definitions surrounding diarrhea in young children, identified 12 local terms for types of diarrheal illness, and pre-existing beliefs about care-seeking and the need for ORS varied for each type [38]. In India, the term *pani ki kami* is often used to describe children with diarrhea. In this study, data on *pani ki kami* were collected but were not used for this analysis because, although highly correlated with report of sunken eyes and lethargy, the term was not considered a reliable indicator of dehydration from a medical standpoint. Further research is necessary to determine whether locally recognized terms for diarrheal severity and symptoms influence recall, care-seeking and ORS/zinc treatment in rural villages in Bihar, Gujarat and UP, India.

An additional study limitation is the use of prompted as opposed to open-ended questions to assess the presence of diarrheal episode characteristics. Prompted questions make mention of specific symptoms, which may influence responses by either reminding caregivers of symptoms they would have otherwise forgotten or by suggesting the presence of symptoms that never actually occurred. While this methodology may have resulted in higher than expected prevalence of various characteristics (Table 4.5), it is unlikely to have biased the results of the regression analyses unless the influence of prompted questions was differential between caregivers by episode onset, care-seeking, or receipt of ORS/zinc treatment.

Due to the issues of prompted questions and poor specificity of the IMCI criteria [28], the measure of any dehydration may have overestimated the prevalence of dehydration in a community setting where most cases are typically mild or moderate in severity. However, if episodes among sampled children reflect the global proportions of mild, moderate and severe diarrhea, the measure may have been adequate, since the prevalence of any dehydration in these data (25.4%) was approximately equivalent to published estimates of total dehydration prevalence among children with mild, moderate and severe diarrhea globally (23.0%) [17].

The study is also limited by potential misreporting of diarrhea onset and recovery dates. It is unlikely that caregivers recorded these dates on a calendar and thus accurate recall of the specific timing of illness onset and recuperation may have been difficult. Date of onset shows slight peaks at 7 and 14 days prior to the survey (Figure 4.2), illustrating the tendency of respondents to round date estimates to the nearest week. In comparing the relative odds of reported symptoms between episodes with reported onset 7-14 days and <7 days prior to data collection, both peaks are categorized into the former category; however, reanalysis of the data comparing reported onset of 8-14 days with ≤7 days preceding the survey does not alter the results.

Finally, while the overall sampling design and survey methodology were strong, strict timelines precluded repeat visits to specific households with caregivers absent at the time of the interviewers' initial visit. Sole inclusion of caregivers available at the time of the interviewers' visits may contribute to selection bias. However, the village sampling scheme, which included splitting villages into geographic quadrants and systematically visiting households, was designed to limit such bias because missing caregivers were replaced with caregivers with similar socio-demographic characteristics from neighboring households in the same quadrant.

4.4.3 Broader implications and conclusions

This study has implications for the overarching evaluation and for programs aiming to improve the management of diarrhea among children under-five in India. Evaluations should consider that cross-sectional data collection with two-week recall leads to underestimation of two-week diarrhea prevalence and overestimation of the proportion of diarrheal episodes that are severe. A recall interval of one-week as opposed to two-weeks would substantially decrease recall errors and is therefore preferable for evaluations aiming to produce unbiased estimates of program outcomes and impact. While the increases in sample size requirements that result from decreasing the length of the recall interval may not be logistically feasible, evaluators should at the very least collect data on diarrhea onset at the one- and two-week marks in order to estimate the level of recall decay present in the data.

Diarrhea management programs should also remain mindful of the influence of perceived episode severity on care-seeking and ORS/zinc treatment. Ideally, programs should encourage care-seeking and treatment for all diarrheal episodes among children under-five, regardless of severity. However, further research is warranted to ascertain whether the promotion of care-seeking and ORS/zinc treatment for perceivably less severe episodes has a measurable impact on under-five mortality. It is possible that limited programmatic resources are more effectively allocated to the promotion of care-seeking and treatment for episodes exhibiting certain symptoms and characteristics, and future research should therefore outline the specific severity criteria that can be translated into promotional messages for caregivers of children under-five. Still, future evaluation research should also address the possibility that the failure to promote ORS and zinc treatment for perceivably less severe episodes could have negative implications for program outcomes centered on diarrheal morbidity.

This study has highlighted that the factors most highly associated with ORS and zinc treatment were not indicators of perceived severity, but rather state of residence and the sector through which care was sought. The odds of receiving ORS/zinc were elevated among those that sought care through the public as opposed to the private sector in all three states (Tables 4.10-4.11), which suggests that the quality of diarrhea treatment is disparate across different sectors. Moreover, discrepancies in ORS treatment between delivery channels are concerning given that any dehydration was associated with private rather than public sector sources of care-seeking (Table 4.9). The aim of diarrhea management programs should therefore be twofold—to increase public sector care-seeking for diarrhea among children under-five and to improve treatment practices for childhood diarrheal episodes through all commonly utilized sources, including sometimes hard-to-reach informal private sector practitioners, such as RMPs. Meeting these challenges may require strategies tailored to specific state needs; in UP, for example, the odds of seeking care for diarrhea are higher compared to Bihar and Gujarat (Table 4.8), but the relative risk of seeking care through the public versus private sector is lower than that of the other states (Table 4.9). Thus, in a diverse country with a complex health system, such as India, programs cannot rely on the same solution in every context. In the same vein, program evaluations must consider regional differences and set state-specific benchmarks for outcome and impact.

Table 4.1

Required sample sizes of caregivers of children 2-59 months of age by state and evaluation phase.

	Bihar	Gujarat	UP
Baseline [1,2]	2409	4167	3889
Midline [1,3]	-	911	1522

[1] Sample size calculations were conducted in Stata 10.0 with 80% power, 5% type I error and continuity correction [35].

[2] Calculations were for a precision estimate of ORS coverage based on the assumption that baseline ORS coverage was 20.9% in Bihar, 26.3% in Gujarat and 12.5% in UP, and the minimum detectable differences were 14.5% in Bihar, 18.7% in Gujarat and 16.5% in UP. Required sample sizes were doubled to ensure sufficient power to estimate ORS coverage among the lowest two wealth quintiles and were adjusted for the design effect (to account for inter-household correlation) and for two-week diarrhea prevalence.

[3] Calculations were based on a minimum detectable change in ORS coverage from 15.3% in Gujarat and 21.6% in UP to 45% in either state. Required sample sizes were adjusted for the design effect, pre-post correlation and two-week diarrhea prevalence.

Table 4.2

Power* to detect the difference in the proportion of diarrheal episodes with any dehydration comparing reported onset ≥7 days to < 7 days

Minimum detectable difference between $p_{\geq 7\ days}$ and $p_{<7 days}$	**+/- 5%**	**+/- 7%**	**+/- 10%**	**+/- 12%**	**+/- 15%**
Proportion of episodes with any dehydration among those with onset ≥7 days before survey					
0.15	33.8%	56.7%	83.9%	93.5%	98.8%
0.18	30.3%	51.8%	80.0%	91.2%	98.2%
0.21	27.6%	47.9%	76.5%	88.9%	97.5%
0.24	25.6%	44.8%	73.5%	86.8%	96.7%
0.27	24.1%	42.3%	70.9%	85.0%	96.0%

*Estimated power calculated in Stata 12.0 at the alpha=0.05 level for a sample size** of $n_{\geq 7\ days}$=741 and $n_{<7\ days}$=176 [36].

** This analysis was restricted to episodes that were completed at the time of the survey (n=917; see sections 4.2.9 and 4.3.8 for details).

Table 4.3

Power[*] to detect the difference in the proportion of diarrheal episodes for which care was sought comparing any dehydration with no dehydration

Minimum detectable difference between $p_{AnyDehydration}$ and $p_{NoDehydration}$	**+/- 1%**	**+/- 3%**	**+/- 5%**	**+/- 7%**	**+/- 10%**
Proportion of episodes with any dehydration for which care was sought					
0.70	5.9%	25.5%	60.3%	88.4%	99.6%
0.75	6.2%	28.5%	66.3%	92.4%	99.9%
0.80	6.7%	33.2%	74.5%	96.3%	99.98%
0.85	7.6%	41.4%	85.3%	99.1%	99.99%
0.90	9.3%	57.4%	96.4%	99.9%	-

[*]Estimated power calculated in Stata 12.0 at the alpha=0.05 level for a sample size of $n_{AnyDehydration}$ =542 and $n_{NoDehdration}$ =1590 [36].

Table 4.4

Power* to detect the difference in the proportion of diarrheal episodes treated with ORS/zinc comparing any dehydration with no dehydration

Minimum detectable difference between $p_{AnyDehydration}$ and $p_{NoDehydration}$	**+/- 1%**	**+/- 3%**	**+/- 5%**	**+/- 7%**	**+/- 10%**
Proportion of episodes with any dehydration treated with ORS/zinc					
0.05	10.5%	61.9%	96.2%	99.9%	99.99%
0.10	7.8%	41.8%	83.4%	98.3%	99.99%
0.15	6.7%	32.8%	72.1%	94.5%	99.9%
0.20	6.2%	28.0%	64.0%	90.2%	99.6%
0.25	5.9%	25.0%	58.4%	86.3%	99.2%

*Estimated power calculated in Stata 12.0 at the alpha=0.05 level for a sample size of $n_{AnyDehydration}$ =542 and $n_{NoDehdration}$ =1590 [36].

Table 4.5

Reported demographic and diarrheal episode characteristics

	N=2132 n (%)
Demographic characteristics	
Male	1132 (53.1)
Child age	
Mean (SD) in months	18.0 (13.4)
2-11 months	877 (41.1)
12-23 months	639 (30.0)
≥24 months	616 (28.9)
Caregiver education >7 years	406 (19.0)
Diarrheal episode characteristics	
Any dehydration	542 (25.4)
Blood in stools	261 (12.2)
Fever	1541 (72.3)
Vomiting	936 (43.9)
Maximum stool frequency	
Mean (SD) in stools/day	5.6 (2.5)
>5 stools/day	821 (38.5)
Episode duration	
Mean (SD) in days	4.4 (3.9)
>5 days	512 (24.0)
>2 days	1375 (64.5)
Child recovered at time of survey [a]	934 (43.8)

Table 4.5 continued

	N=2132 n (%)
Care-seeking and treatment	
Care-seeking outside the home	1690 (79.3)
Private sector only [b]	1473 (87.2)
Public sector only [b]	98 (5.8)
Public and private sectors [b]	63 (3.7)
Episode treated with ORS	392 (18.4)
Episode treated with zinc	81 (3.8)

[a] Children were considered recovered following a period of 72-hours in which loose or watery stools were not experienced.

[b] The number of caregivers seeking care outside the home (N=1690) was used as the denominator for percentage calculations. The sum of percentages <100% because source of care-seeking was not specified for 56 (3.3%) of care-seekers.

Table 4.6

Diarrheal characteristics associated with more distant recall of diarrhea[*] in bivariate analyses[**]

	Unadjusted OR[**]	95% CI	P-value
Any dehydration	1.59	1.09-2.33	0.017
Blood in stools	2.02	1.11-3.70	0.022
Fever	1.72	1.18-2.50	0.005
Vomiting	1.80	1.29-2.53	0.001
Maximum stool frequency >5 stools/day	2.01	1.34-3.02	0.001

[*] Outcome variable was defined as reported diarrhea onset 7-14 days prior to the survey (i.e. more distant recall) compared to 3-6 days prior to the survey (i.e. more recent recall).

[**]Bivariate analyses were performed in Stata 12.0 using logistic regression with the robust cluster estimator of variance to account for intra-village correlation [36].

Table 4.7

Factors associated with more distant recall of diarrhea* in multivariable analysis**

	Adjusted OR**	95% CI	P-value
Any dehydration	1.29	0.84-1.98	0.240
Blood in stools [a]			
At duration >2 days	8.03	1.08-59.54	0.041
At duration = 1-2 days	0.75	0.33-1.73	0.503
Fever	1.23	0.81-1.88	0.323
Vomiting	1.26	0.87-1.84	0.221
Maximum stool frequency			
>5 stools/day	1.07	0.68-1.68	0.779
≤5 stools/day	1.0		
Episode duration [a]			
Blood in stools	49.19	5.39-448.91	0.001
No blood in stools	4.71	3.10-7.15	<<0.001
Child age			
>23 months	0.85	0.58-1.26	0.424
≤ 23 months	1.0		
Child gender			
Male	1.02	0.73-1.42	0.910
Female	1.0		

Table 4.7 continued

	Adjusted OR**	95% CI	P-value
Caregiver education			
>7 years	0.70	0.45-1.08	0.107
≤7 years	1.0		
State			
Gujarat	0.74	0.44-1.25	0.257
UP	0.79	0.47-1.33	0.379
Bihar	1.0		

[*] Outcome variable was defined as reported diarrhea onset 7-14 days prior to the survey (i.e. more distant recall) compared to 3-6 days prior to the survey (i.e. more recent recall).

[**] Multivariable logistic regression analysis was performed in Stata 12.0 using the robust cluster estimator of variance to account for intra-village correlation [36].

[a] There was a statistically significant interaction between the binary variables for blood in stools and episode duration>2 days (p=0.038).

Table 4.8

Factors associated with diarrhea care-seeking in multivariable analysis*

	Adjusted OR*	**95% CI**	**P-value**
Any dehydration	1.68	1.19-2.36	0.003
Blood in stools	1.26	0.84-1.88	0.265
Fever	2.31	1.79-3.00	<<0.001
Vomiting	1.85	1.41-2.43	<<0.001
Maximum stool frequency			
>5 stools/day	1.79	1.33-2.42	<<0.001
≤5 stools/day	1.0		
Episode duration (days)	1.09	1.03-1.15	0.003
Recovered at time of survey	4.04	2.99-5.45	<<0.001
Child age (months)	1.01	1.00-1.02	0.298
Child gender			
Male	1.17	0.93-1.48	0.185
Female	1.0		
Caregiver education			
>7 years	1.27	0.911-1.77	0.158
≤7 years	1.0		
State			
UP	2.26	1.64-3.12	<<0.001
Bihar	1.56	1.08-2.26	0.018
Gujarat	1.0		

* Analysis was performed in Stata 12.0 using multivariable logistic regression with the robust cluster estimator of variance to account for intra-village correlation [36].

Table 4.9

Factors associated with where care was sought in multinomial regression analysis*

	Public sector only vs. private sector only Adjusted RRR (95% CI)*	**Both sectors vs. private sector only Adjusted OR (95% CI)***
Any dehydration	0.56 (0.32-0.98)	0.85 (0.46-1.57)
Maximum stool frequency (stools/day)	1.02 (0.92-1.13)	1.15 (1.06-1.25)
Episode duration (days)	0.96 (0.89-1.05)	1.03 (0.95-1.11)
Recovered at time of survey	1.17 (0.78-2.45)	1.52 (0.87-2.66)
Child age (months)	1.02 (1.00-1.04)	1.01 (0.99-1.02)
Child gender		
Male	0.66 (0.42-1.02)	1.04 (0.65-1.68)
Female	1.0	1.0
Caregiver education		
>7 years	1.38 (0.78-2.45)	0.55 (0.24-1.27)
≤7 years	1.0	1.0
State		
Gujarat	6.62 (3.72-11.80)	6.83 (3.28-14.20)
Bihar	1.37 (0.63-2.97)	2.06 (0.88-4.78)
UP	1.0	1.0

* Multinomial logistic regression analysis was performed in Stata 12.0 to model the categorical dependent outcome variable of where care was sought: 0=private sector only; 1=public sector only; 2=both sectors. The robust cluster estimator of variance was employed to account for intra-village correlation [36].

Table 4.10

Factors associated with ORS treatment of diarrhea in multivariable analysis*

	Adjusted OR*	95% CI	P-value
Any dehydration at child age=2 months [a]	1.60	1.10-2.34	0.015
Blood in stools	0.85	0.60-1.19	0.343
Fever	0.93	0.67-1.28	0.653
Vomiting	1.85	1.43-2.39	<<0.001
Maximum stool frequency			
>5 stools/day	1.53	1.20-1.95	0.001
≤5 stools/day	1.0		
Episode duration (days)			
>2 days	1.07	0.80-1.43	0.644
1-2 days	1.0		
Recovered at time of survey	1.43	1.11-1.84	0.006
Child age centered at 2 months [b]			
Any dehydration	0.98	0.96-0.99	0.12
No dehydration	1.00	0.99-1.01	0.932
Child gender			
Male	1.10	0.86-1.40	0.462
Female	1.0		

Table 4.10 continued

	Adjusted OR*	95% CI	P-value
Caregiver education			
>7 years	1.35	1.02-1.80	0.036
≤7 years	1.0		
Care sought through public versus private sector [b]			
Gujarat	4.73	2.86-7.84	<<0.001
Bihar	4.40	1.77-10.93	0.001
UP	1.22	0.55-2.69	0.623

* Analysis was performed in Stata 12.0 using multivariable logistic regression with the robust cluster estimator of variance to account for intra-village correlation [36].

[a] Analysis controlled for interaction between the binary variable for any dehydration and the continuous variable for child age centered at 2 months. The adjusted OR of ORS treatment among dehydrated children 2 months of age is 1.60 (95% CI: 1.10-2.34), which decreases by 2.1% (95% CI: 0.5-3.7%) per one month increase in age, holding all other variables constant.

[b] Analysis controlled for interaction between indicator variables for state and the binary variable for where care was sought (1=any public sector care-seeking; 0=private sector only).

Table 4.11

Factors associated with zinc treatment of diarrhea in multivariable analysis*

	Adjusted OR*	**95% CI**	**P-value**
Any dehydration	0.97	0.57-1.63	0.90
Blood in stools	0.86	0.44-1.70	0.664
Fever	0.90	0.51-1.60	0.725
Vomiting	0.90	0.56-1.45	0.667
Maximum stool frequency			
>5 stools/day	1.71	1.05-2.79	0.030
≤5 stools/day	1.0		
Episode duration (days)			
>2 days	1.12	0.68-1.83	0.659
1-2 days	1.0		
Recovered at time of survey	1.73	0.97-2.46	0.064
Child age (months)	0.99	0.98-1.01	0.393
Child gender			
Male	1.55	0.97-2.46	0.064
Female	1.0		

Table 4.11 continued

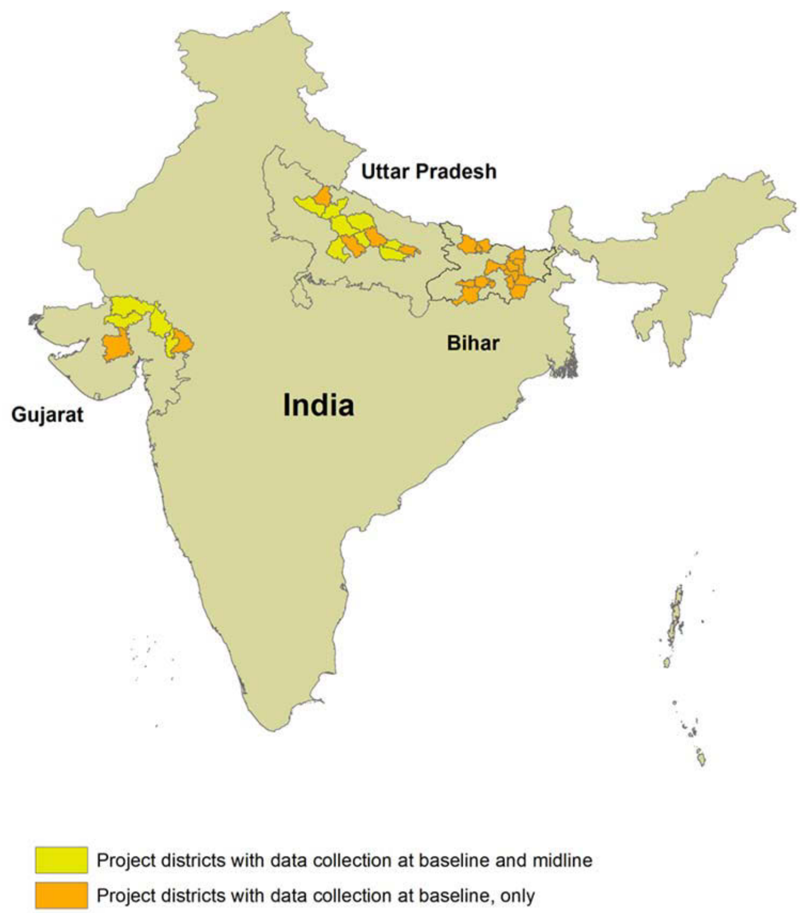
	Adjusted OR*	95% CI	P-value
Caregiver education			
>7 years	1.19	0.67-2.12	0.556
≤7 years	1.0		
Care sought through public versus private sector [a]			
Gujarat	8.85	3.32-23.57	<<0.001
Bihar	20.3	5.60-73.58	<<0.001
UP	2.12	0.60-7.52	0.247

* Analysis was performed in Stata 12.0 using multivariable logistic regression with the robust cluster estimator of variance to account for intra-village correlation [36].

[a] Analysis controlled for interaction between indicator variables for state and the binary variable for where care was sought (1=any public sector care-seeking; 0=private sector only).

Figure 4.1

Districts included at the baseline and midline phases of the evaluation by state [a, b]



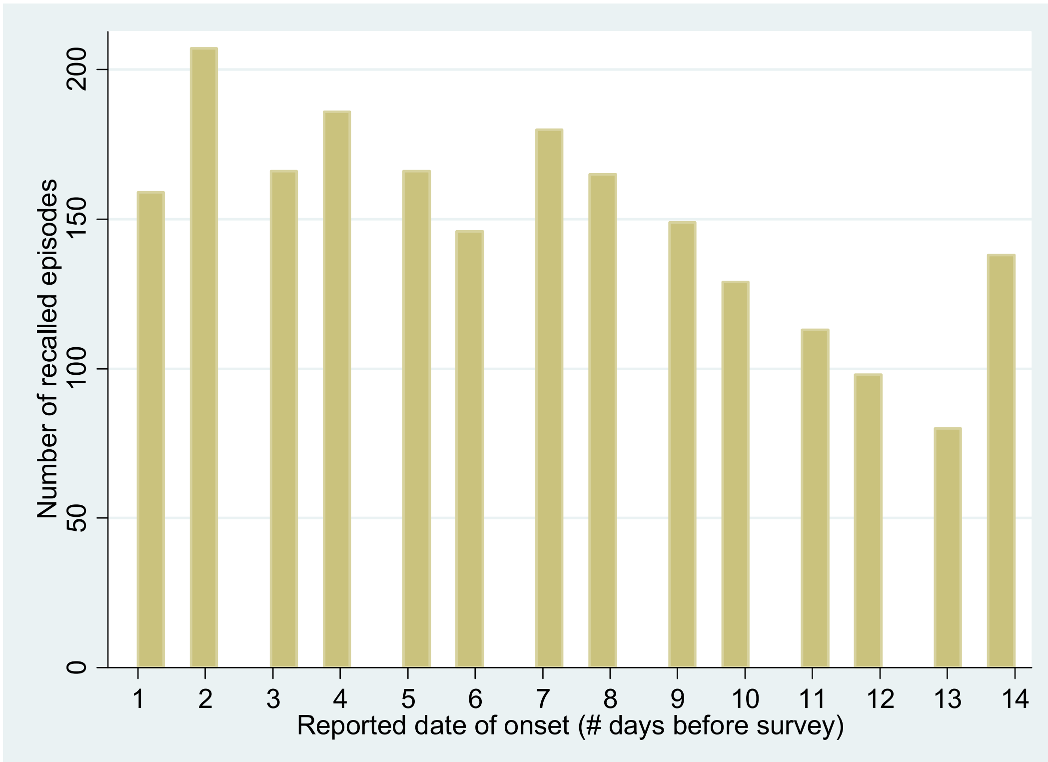
<u>Source</u>: Map was generated using ArcGIS software and DIVA-GIS shapefiles [39, 40].

[a] Data collection at baseline and midline in 8 districts in UP (*Badaun, Faizabad, Hardoi, Kanpur Dehat, Lucknow, Shahjahanpur, Sitapur, Sultanpur*) and 4 districts in Gujarat (*Banas Kantha, Panch Mahals, Patan, Sabar Kantha*). Data collection at only baseline in 15 districts in Bihar (*Banka, Bhagalpur, East Champaran, Gaya, Jehanabad, Khagaria, Madhepura, Munger, Nalanda, Saharsa, Samastipur, Sheikhpura, Sheohar, Sitamarhi, Supaul*), 4 districts in UP (*Ambedkar Nagar, Bara Banki, Bareilly, Unnao*) and 2 districts in Gujarat (*Dohad, Surendranagar*).

[b] Program implemented in the public and private sectors of Gujarat and UP and the public sector alone in Bihar.

Figure 4.2

Distribution of recalled diarrheal episodes* by reported date of onset**

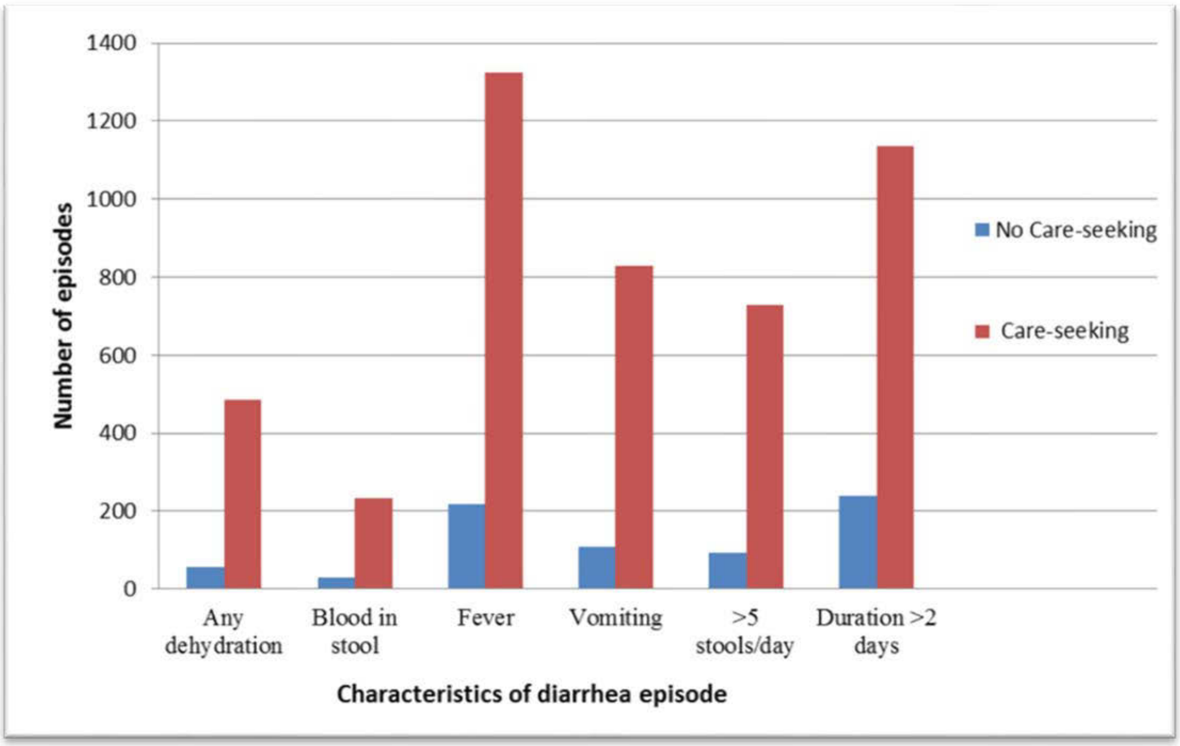


* N= 2,132 episodes.

** Episodes with reported onset on the day of the survey were combined with those starting 1 day before the survey, since the survey date was not a full day of observation.

Figure 4.3

Trends in care-seeking among children with reported diarrheal characteristics



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Chapter Five: Paper 3

ORS and zinc supplementation for the treatment of childhood diarrhea in Bihar, Gujarat and Uttar Pradesh, India: the association between provider knowledge and practice

5.1 Introduction

5.1.1 The burden of diarrhea among children under-five in Bihar, Gujarat and Uttar Pradesh, India

In India, approximately 212,000 deaths among children under-five were attributable to diarrhea in 2010 [1]. While this figure has decreased substantially from over 0.5 million in 2004 [2], India continues to rank first on the list of childhood diarrheal deaths as more children die from diarrhea in India than in any other country in the world [1]. Though a nationwide problem, diarrheal mortality rates are highest in rural areas and in states characterized by less wealth and development and high birth rates [3, 4]. Among children under five years of age, the 2005 diarrheal mortality rates were 14.5, 12.6 and 4.9 deaths per 1000 live births in the Central, East and West regions of India, respectively [3]. Uttar Pradesh (UP), located in the Central region, and Bihar, located in the East, rank first and second among all Indian states in terms of the highest crude number of annual diarrheal deaths among children under-five [4, 5]. In comparison to UP and Bihar, Gujarat—a state in the Western region of India, has higher GDP per capita and lower under-five mortality [4, 6]. Elevated levels of diarrheal morbidity affect children under-five years of age throughout India and in the states of Bihar, UP and Gujarat [7]. As estimated by the National Family Health Survey-3 (NFHS-3), the two-week prevalence of diarrhea among children under-five was 9% nationally, 13% in Gujarat, 11% in Bihar and 8% in UP in 2005-2006 [7-10].

5.1.2 The treatment of childhood diarrhea in India

The World Health Organization (WHO) and UNICEF recommend the use of reduced osmolarity oral rehydration salts (ORS) solution and therapeutic zinc supplementation for the treatment of diarrhea among children under-five globally [11]. There is a large body of evidence supporting the use of reduced osmolarity ORS to prevent and treat diarrhea-associated dehydration and death [12]. In addition, 10-14 days of supplementation with 20 mg of zinc/day for children ≥ 6 months and 10 mg of zinc/day for infants <6 months has been shown to reduce the duration, severity and recurrence of diarrheal episodes among children under-five [13]. In 2003 and 2006, the Government of India and the Indian Academy of Pediatrics issued revised national recommendations for the treatment of childhood diarrhea, which included reduced osmolarity ORS for all children under-five and 20 mg/10 mg of zinc per day for 14 days for children 7-59 months/2-6 months of age [14, 15].

5.1.3 Increasing access to adequate diarrhea treatment through the Indian health system

National efforts to control childhood diarrhea in India have focused on increasing access to adequate treatment through public sector channels [16]. The public sector consists of district-level hospitals, community health centers (CHC), primary health centers (PHC) and sub-health centers (SHC); district hospitals, CHCs and SHCs attend to populations of 2-3 million, 100,000-300,000, and 5,000, respectively [17]. The population covered by PHCs varies by state, ranging from 30,000 in less populated states to 150,000 in the most populated state, UP. Providers at all levels of the public health system play a role in managing diarrhea among children under-five: medical officers are essential to the treatment of severe cases seeking care at facilities; whereas, auxiliary nurse midwives and Accredited Social Health Activists (ASHAs) undertake child health activities in villages and are therefore vital to early detection and prompt treatment of diarrhea cases occurring in the community. Anganwadi workers (AWWs), which are generally responsible for pre-school education and other health mobilization activities, are also positioned to treat diarrhea in the community. AWWs have not typically dispensed medical treatment, but several state governments have issued stipulations that permit AWWs to distribute ORS and zinc for diarrhea treatment.

Despite national and state efforts encouraging utilization of public sector services for diarrheal treatment, about 80% of care-seeking for diarrhea takes place through the private sector [7, 18]. The Indian private health sector consists of formally qualified medical doctors, as well as informal providers referred to as rural medical practitioners (RMPs). The term RMP is loosely used to refer to several provider types, including those with government-recognized degrees in modern allopathic/traditional *'Ayush'* (Ayurveda, Unani, Siddha, Homeopathy) medicine and those lacking formal training [18-20]. The majority of RMPs are unqualified and unregulated, falling under the latter category; however, their services fill a gap in rural communities isolated from the government health system [18, 20]. Consequently, RMPs and other private practitioners play a significant role in treating childhood diarrhea in India, but they typically prescribe injections, antibiotics and anti-diarrheal medications rather than ORS and zinc [18-20]. In order to leverage the position of RMPs in the community, diarrhea management programs must focus on improving the proportion of RMPs that adequately treat diarrhea among children under-five.

5.1.4 Diarrhea management programs in Bihar, Gujarat and Uttar Pradesh, India

In the fall of 2010, the Bill and Melinda Gates Foundation (BMGF) funded the Diarrhea Alleviation through Zinc and ORS Treatment (DAZT) program in Uttar Pradesh and Gujarat, India. Micronutrient Initiative (MI) and FHI 360 were contracted to implement activities in the public and private health sectors, respectively. The Johns Hopkins University Institute for International Programs (JHU IIP) and the Society for Applied Studies (SAS) in New Delhi were appointed to conduct a large-scale effectiveness evaluation of the program in both states. Simultaneously, the Children's Investment Fund Foundation (CIFF) pledged support for a similar program solely focused on the public sector in Bihar. The Bihar program was also implemented by MI and evaluated by JHU IIP/SAS.

5.1.5 The association between diarrhea management knowledge and practice among ASHAs, AWWs and RMPs in Bihar, Gujarat and Uttar Pradesh, India

In India, the success of diarrhea management programs is largely dependent on the practices of community-level public- and private-sector providers, such as ASHAs, AWWs and RMPs. Diarrhea management programs often focus on training such providers in an effort to increase their knowledge of adequate childhood diarrhea management, including ORS and zinc. However, increasing provider knowledge is not sufficient to improve childhood diarrhea outcomes if improved knowledge does not translate into improved practice. One study of mothers of children under-five in the Gambia reported that despite high levels of knowledge, utilization of ORS to treat diarrhea among young children was low [21]. A pre- and post-educational intervention study among pharmacy workers in Vietnam found that high levels of reported knowledge were not necessarily correlated with adequate diarrhea prescribing practices during simulated patient consultations [22].

Thus, research is warranted to assess the association between observed childhood diarrhea prescribing practices and reported knowledge of ORS and zinc among RMPs, ASHAs and AWWs in UP, Gujarat and Bihar, India. Comparisons between reported knowledge and observed prescribing of ORS and zinc can shed light on the factors influencing providers to advise proper diarrhea treatment to children under-five years of age in the community. Specifically, this analysis will help determine the role of provider knowledge in prescribing diarrhea treatment for children under-five and will thus dictate the relative importance of investments in RMP, ASHA and AWW training and educational materials in the grand scheme of diarrhea management programs.

5.2 Methods

5.2.1 Sampling Design and Sample Size Requirements

Cross-sectional assessments were conducted on informal private sector RMPs in UP and public sector ASHAs and AWWs in Bihar and Gujarat. The study was carried out in all districts in which the first phase of the DAZT and CIFF programs were rolled-out, including 5 districts in Bihar, 4 districts in Gujarat and 12 districts in UP. In the public sector, a multi-stage cluster sampling design was employed in which PHCs and providers comprised the primary and secondary sampling units, respectively. A total of 33-35 PHCs were randomly selected in each state based on probability proportional to size (PPS) sampling, such that the proportion of PHCs sampled from each district equaled the proportion of PHCs in that district relative to the total across all selected districts in a given state (Table 5.1).

In the public sector, sample size requirements were calculated for one of the main evaluation outcomes—the proportion of ASHAs and AWWs that prescribe ORS for diarrhea among children under-five. Using the assumption that 10% of ASHAs/AWWs advised ORS to treat diarrhea, sample size requirements were calculated in Stata 12.0 to determine the true proportion of ASHAs/AWWs advising ORS to treat under-five diarrheal episodes within a 10% margin of error and 80% power at the alpha=2.5% level, accounting for the Bonferroni correction to allow comparisons between ASHAs and AWWs, the design effect and missingness (Table 5.2) [23]. A total sample size of 165 ASHAs and 165 AWWs was required for each state; 4-5 ASHAs and 4-5 AWWs were randomly selected from each PHC in Gujarat and Bihar.

In the private sector, a multi-stage cluster sampling design was also employed; tehsils, a geographic unit in UP, comprised the primary sampling units and RMPs were the secondary sampling units. A total of 29 tehsils were randomly selected based on PPS sampling, such that the proportion of tehsils sampled from each district equaled the proportion of the informal provider population operating in that district relative to the total population across all 12 selected districts (Table 5.3). Sample size requirements for RMPs were based on zinc, rather than ORS, prescribing because RMPs do not commonly advise ORS. Under the assumption that 10% of RMPs always prescribed zinc for childhood diarrhea, a sample size of 146 RMPs was required to detect the true proportion ± 10% with 80% power at the alpha=5% level, accounting for the design effect and missingness (Table 5.4).

Random selection of PHCs and tehsils were carried out in advance of the survey using Stata 12.0 statistical software before the field staff shifted to the districts [23]. The selection of ASHAs and AWWs was conducted in the field by study coordinators who were responsible for contacting PHC administrators to obtain an up-to-date list of current employees; all current ASHAs and AWWs were eligible for inclusion in the study. Coordinators then utilized these lists to randomly select ASHAs and AWWs using a pre-determined selection scheme in which PHCs were assigned a random letter of the English alphabet and providers were chosen alphabetically starting with the assigned letter. Using Stata 12.0 statistical software, RMPs were randomly selected from a sampling frame of informal private sector providers that had been identified by FHI360 [23]. In the event that a randomly selected provider could not be reached after three attempts, researchers at headquarters randomly selected additional PHCs and tehsils/RMPs in the same district as the missing provider, and the deficit was made up at the district level.

5.2.2 Interviewer Training

Interviewers received thorough training in New Delhi before implementation of any field activities. The training entailed classes, mock interviews, form filling and a review of the logistics of field operations. Additionally, supervisors held refresher trainings periodically while stationed in the field.

5.2.3 Ethical Approval

Field staff obtained informed consent from selected providers and verbal assent from the caregivers of children observed during provider consultations. Ethical approval was obtained from the Johns Hopkins University Institutional Review Board (IRB) in Baltimore, MD and from the Society for Applied Studies Ethical Review Committee (ERC) in New Delhi, India prior to data collection activities. The governments of Bihar and Gujarat also granted written approvals permitting interviews with government-employed public sector workers.

5.2.4 Data Collection

Data were collected from October-November 2011 in Bihar, December 2011 – January 2012 in Gujarat, and June-July 2012 in UP. The provider assessment included two parts: 1) an observation of the provider in consultation with one eligible diarrhea case and 2) a 45-minute interview. The observation was conducted first to prevent biasing the provider's behavior with the content of the interview questions. Children eligible for observation were 2-59 months of age and suffering from a current, untreated diarrheal episode as defined by passage of at least three loose/watery stools in the previous 24 hours. In order to identify such cases during the public sector assessments, interviewers accompanied ASHAs and AWWs during their routine visits in the community and enrolled the first child meeting the eligibility criteria. During the private sector assessment, interviewers waited for a period of one working day at the selected RMP's practice, and the first child seeking care and meeting the eligibility criteria was enrolled.

Children were excluded if they had already received treatment outside the home for the current diarrheal episode and/or their caregiver did not verbally consent.

Once a consenting, eligible child was identified, interviewers observed the routine treatment practices of providers. Using an observation form specifically designed for this study, interviewers silently noted whether the provider asked the caregiver about diarrheal symptoms and episode duration. The interviewer also recorded any treatments recommended or provided during the consultation, as well as specific instructions on their usage (e.g. ORS preparation and zinc dosage). If a child eligible for observation was not identified during the ASHA/AWW's routine visits or within 24-hours of waiting at the RMP practice, the interviewer skipped the observation and proceeded with the survey portion of the assessment. Following the observation, providers were interviewed in a private location. The interview lasted about 30 minutes and included questions on knowledge of diarrhea management, practices and access to routinely available ORS and zinc supplies.

5.2.5 Quality Control

Coordinators checked forms for accuracy nightly, and inconsistencies were resolved in the field. Data were entered into predesigned databases and cleaned at SAS headquarters in New Delhi.

5.2.6 Power Calculations

During data collection, a total of 97 RMPs, 330 ASHAs, and 330 AWWs were both interviewed and observed during a treatment interaction with an eligible diarrhea case (Table 5.5). It was not possible to observe all of the RMPs enrolled in the study because care-seeking for diarrhea at RMP practices was lower than anticipated, and an eligible child was not always present on the day of the study visit. Table 5.5 describes the number of observations and interviews achieved by state and provider type.

In Stata 12.0, the number of achieved observations was used to calculate the power achieved to detect the proportion of RMPs and ASHAs/AWWs that prescribed both ORS and zinc to treat diarrhea among children under-five (p) [23]. Table 5.6 presents the estimated power at the alpha=0.05 level under a range of margins of error and a range of values for p; for ASHAs and AWWs, a slightly higher range of values for p was used, since these providers generally prescribed ORS and zinc in higher proportions than RMPs. These calculations confirm that power was adequate to achieve the study aims.

5.2.7 Construction of Knowledge Indexes

This study sought to determine whether provider knowledge of ORS and zinc could be used to predict ORS and zinc prescribing practices during observed treatment consultations. The first step in achieving this aim was to construct a scale to quantify providers' reported knowledge of ORS and zinc treatment for diarrhea among children 2-59 months of age. Provider survey responses on zinc and ORS use, zinc dose and duration, and ORS preparation were used to generate a set of binary variables equal to 1 for correct responses and 0 for incorrect responses (Table 5.7). Principal components analysis (PCA) was conducted on these variables in Stata 12.0 in order to construct three separate indexes: 1) a zinc knowledge index; 2) an ORS knowledge index; and 3) a combined zinc and ORS knowledge index [23].

PCA is a method by which a set of correlated variables is reduced to a set of uncorrelated weighted linear combinations of the original variables [24]. PCA assigns a weight (also known as factor score) to each of the original variables, which is based upon the ability of that variable to explain variability across responses [24]. In other words, in constructing the knowledge indexes, higher PCA weights are allocated to variables derived from the survey questions that best differentiate providers with high and low knowledge. For example, if the majority of providers answer 6 out of 7 zinc knowledge questions correctly, variability in zinc knowledge is best assessed by responses to the 7th question and that question will receive a higher PCA weight. Accordingly, variables with large splits in the frequency of correct and incorrect responses will be allocated higher PCA weights than more evenly distributed variables. The PCA weights thus provide an alternative to uniformly assigning the same weight to all variables, which is a more simplistic approach to gauging knowledge.

In order to calculate the knowledge index score for each provider, the PCA weights were substituted into the following formula using Stata 12.0 [23, 25]:

$$A_i = \sum_n f_n \left(\frac{a_{in} - \overline{a_n}}{s_n} \right)$$

According to this formula, the knowledge index score (A) for provider i equals the summation over n knowledge variables of the PCA weight for a given knowledge variable (f_n) multiplied by the standardized value of that knowledge variable for provider i; the standardized value of the knowledge variable is equal to the value of the knowledge variable for provider i (a_{in}) minus the mean value of the knowledge variable across all providers ($\overline{a_n}$), divided by the standard deviation of the knowledge variable (s_n).

To further clarify calculation of the knowledge index score, consider the example of hypothetical provider i who has incorrectly responded to all three knowledge questions on a hypothetical survey and resultantly has values of 0 for all three variables used to construct the hypothetical knowledge index score. In addition, assume that the means and standard deviations of the three variables across all surveyed providers are 1, 2, 3 and 3, 2, 1, respectively, and that the PCA weights for the three variables are -1, 0.5 and 1. The knowledge index score for provider i would be calculated as follows:

$$A_i = -1 * \left(\frac{0-1}{3}\right) + 0.5 * \left(\frac{0-2}{2}\right) + 1 * \left(\frac{0-3}{1}\right)$$

Although PCA was designed for use with continuous normally-distributed variables [26], its application to binary and dichotomized variables is pervasive, especially for the purpose of constructing asset indexes. Based on the aforementioned formula, the index score should be a standardized, continuous random variable with mean equal to zero and standard deviation equal to one [24]; however, when binary or dichotomized variables are used to construct the index, the distributions of resulting scores may be positively- or negatively- skewed. Despite this limitation, PCA is a powerful tool for deriving scales to assess concepts, such as wealth and knowledge

5.2.8 Data Analysis

The data were analyzed with the goal of assessing the relationship between the ORS/zinc/combined knowledge index scores and the outcomes of ORS prescribing, zinc prescribing, and combined ORS and zinc prescribing. Using data from the direct observation of each provider during a treatment interaction with a diarrhea case, binary variables were constructed for the ORS/zinc prescribing outcomes. Prescribing was defined as having advised a specified treatment regardless of whether the product was directly provided during the consultation or advised through another channel.

For the public and private sectors, three separate sets of multiple logistic regression models were fitted for the log odds of observed zinc prescribing, the log odds of observed ORS prescribing, and the log odds of observed ORS and zinc prescribing using Stata 12.0 [23]. All models included the relevant knowledge index score as the primary predictor variable and controlled for whether the provider had access to zinc and/or ORS supplies at the time of the observation. Bivariate analyses were conducted to identify additional covariates for inclusion in the multiple logistic regression models. The variables included in the final public and private sector models are outlined in Table 5.8. Models for both sectors included indicators of child age and gender, provider education, and receipt of diarrhea management training in the 6 months prior to the survey. Additionally, provider type (i.e. ASHA or AWW) and state (i.e. Bihar or Gujarat) were included in public sector models. The public sector models were also inspected for interaction between state and access to ORS/zinc supplies using Wald tests of statistical significance. All regression analyses employed the robust cluster estimator of variance, where PHC was the cluster variable for public sector models and tehsil was the cluster variable for private sector models.

5.3 Results

5.3.1 Provider characteristics and prescribing practices

Table 5.9 outlines key demographic characteristics of the included providers. As expected, all AWWs and ASHAs were female and all RMPs were male. On average, AWWs and ASHAs had 10 years of education and RMPs had 12 years of education. The majority of providers reported having attended diarrhea management training in the 6 months prior to the survey (i.e. 90% AWWs; 89% ASHAs; 69% RMPs).

At the time of the survey, both ORS and zinc supplies were accessible to 39%, 55% and 34% of AWWs, ASHAs and RMPS, respectively. During direct observation, zinc and ORS were prescribed by more than 65% of AWWs and nearly 78% of ASHAs; 19.6% of RMPs advised both ORS and zinc during direct observation. ORS was prescribed without zinc by 28 (8.5%) AWWs, 21 (6.4%) ASHAs, and 36 (37.1%) RMPs. Zinc was prescribed without ORS by 2 (0.6%) ASHAs and 8 (8.2%) RMPs.

5.3.2 Knowledge Index Scores

Table 5.9 lists the proportion of providers that responded correctly to each question included in construction of the index scores. Table 5.10 summarizes the PCA-derived weights (f_n) that were applied to each variable during construction of knowledge indexes for the public and private sectors. The positive value of all weights indicates that correct responses to all knowledge questions were associated with higher knowledge index scores. Higher weights were applied to questions with greater variability across responses (i.e. questions that differentiated between providers with high and low levels of ORS, zinc or combined ORS and zinc knowledge). For example, knowledge of the correct duration of zinc treatment received the highest weight in construction of the zinc knowledge index score for the public sector (weight=0.71); therefore, knowledge of zinc duration can be used to differentiate high and low achievers as explained in section 5.2.7.

All of the zinc, ORS and combined knowledge index scores had means of approximately zero and standard deviations equal to one. Figures 5.1 and 5.2 illustrate the distributions of knowledge index scores among ASHAs/AWWs and RMPs using box plots, which are centered on the mean (i.e. approximately zero) and display a horizontal line at the median. In general, the distributions of knowledge index scores were approximately normal but indicated slight negative skew among ASHAs/AWWs and slight positive skew among RMPs (Figures 5.1 and 5.2). These skew patterns indicate that providers achieving low knowledge scores were outliers among public sector ASHAs/AWWs; whereas, RMPs with high scores deviated from the expected level of knowledge of their counterparts.

5.3.3 Public Sector Regression Analyses

The odds ratios for all variables included in the three public sector regression models are summarized in Table 5.11. The adjusted odds of zinc prescribing were about two-fold higher per point increase in the zinc knowledge index score (aOR: 2.14; 95% CI: 1.70-2.70); the adjusted odds of ORS prescribing were 54% higher per unit increase in the ORS knowledge index score (aOR: 1.54; 95% CI: 1.24-1.92); and the adjusted odds of prescribing both ORS and zinc were elevated by a factor of 2.48 per unit increase in the combined ORS and zinc knowledge index score (aOR: 2.48; 95% CI: 1.90-3.24).

In all three models, the adjusted odds of prescribing were higher among ASHAs compared to AWWs, providers with access to ORS/zinc at the time of the survey, and providers that had received diarrhea management training in the 6 months prior to the survey. There was a non-statistically significant trend towards increased adjusted odds of prescribing among ASHAs/AWWs with >10 years of education. The adjusted odds of prescribing zinc were reduced by 48% (95% CI: 11-69%) for children ≤6 months compared to those 7-59 months of age, and a similar trend was observed for ORS prescribing (aOR: 0.66; 95% CI: 0.40-1.10). Compared to Gujarat, the adjusted odds of zinc prescribing were elevated by a factor of 3.14 (95% CI: 1.56-6.34) in Bihar, but state was not a statistically significant predictor of ORS prescribing. The models did not show evidence of an interaction between state and access to ORS/zinc supplies.

5.3.4 Private Sector Regression Analyses

Table 5.12 summarizes the odds ratios for all variables included in the three private sector regression models. The adjusted odds of zinc prescribing increased by a factor of 3.57 (95% CI: 2.08-6.13) per unit increase in the zinc knowledge index score; the adjusted odds of ORS prescribing were elevated by 28% per unit increase in the ORS knowledge index score (aOR: 1.28; 95% CI: 0.79-2.07); and the adjusted odds of prescribing both ORS and zinc increased by a factor of 2.32 (95% CI: 1.29-4.17) per one-point increase in the combined ORS and zinc knowledge index score.

Access to ORS supplies at the time of the survey was associated with higher adjusted odds of prescribing ORS (aOR: 8.56; 95% CI: 2.81-26.11), but access to zinc supplies did not have an effect on zinc prescribing (aOR: 0.60; 95% CI: 0.16-2.26).

Receipt of diarrhea management training in the 6 months prior to the survey did not have a statistically significant effect on prescribing zinc (aOR: 1.61; 95% CI: 0.45-5.71), ORS (aOR: 0.96; 95% CI: 0.33-2.76) or both zinc and ORS (aOR: 0.88; 95% CI: 0.24-3.25). The adjusted odds of prescribing zinc were 4.24 times higher (95% CI: 1.34-13.40) among RMPs with >14 years of education; however, education did not have an effect on ORS prescribing (aOR: 0.62; 95% CI: 0.21-1.82). In all three models, there was a non-statistically significant trend towards higher odds of prescribing ORS/zinc for children ≤6 months compared to 7-59 months of age.

5.4 Discussion

The practice of advising zinc and ORS for diarrhea treatment among children under-five was positively influenced by zinc and ORS knowledge as measured by a novel scale. In the construction of the knowledge score indexes, greater PCA weights were awarded to survey items with highly variable responses across providers in order to best differentiate those with high and low levels of zinc and ORS knowledge. The most heavily weighted items differed between the public and private sector indexes (Table 5.10): accurate knowledge of zinc dose and duration and of the need to advise ORS for persistent and bloody diarrhea received the greatest weights in the construction of the public sector indexes; in construction of the private sector indexes, the greatest weights were awarded to accurate knowledge of the need to advise zinc and ORS for mild and severe diarrheal episodes.

Receipt of training in the 6 months prior to the survey was associated with higher odds of ORS and zinc prescribing among ASHAs and AWWs regardless of knowledge score (Table 5.11), suggesting the importance of periodic reinforcement of diarrhea management curriculum even among providers with high knowledge of ORS and zinc. As such, diarrhea management programs should schedule biannual refresher trainings for all ASHAs and AWWs.

Training of private sector RMPs, on the other hand, had no effect on observed prescribing practices after controlling for knowledge and other factors (Table 5.12). Unlike public sector providers, RMPs were not formally trained but instead received visits from pharmaceutical or NGO representatives promoting adequate treatment of childhood diarrhea while simultaneously soliciting sales of zinc and ORS. It is probable that most representatives interacted with RMPs for only minutes; whereas, diarrhea management training of ASHAs and AWWs was comprised of formal class sessions lasting hours. It is therefore conceivable that the nature of RMP training precluded a measurable association with prescribing practices. In addition, the small number of RMPs that reported receiving training in the 6 months prior to the survey may have also prevented an association. The small sample size of trained RMPs may be indicative of the hurdles pharmaceutical and NGO representatives encountered when attempting to reach RMPs, since these informal practitioners often operate underground in an attempt to evade government regulations. It is also possible that RMPs had poor recall of visits to their practices, which were of short duration and may not have been especially memorable. These findings suggest that the current structure of RMP training is not effective. Still, it is improbable that communal diarrhea management training sessions, which have had demonstrated impact on prescribing practices among public sector ASHAs and AWWs, would be logistically feasible for RMPs. Further research is warranted to assess whether changing the structure or increasing the duration and/or frequency of one-on-one RMP training sessions can improve RMP prescribing practices for diarrhea among children under-five.

The odds of prescribing ORS and zinc were highly elevated among ASHAs and AWWs with direct access to ORS and zinc supplies, controlling for knowledge score and other factors (Table 5.11). In the event of stock-outs, ASHAs and AWWs are trained to prescribe ORS and zinc anyway and to advise caregivers to obtain these products through alternate channels. However, this finding demonstrates that ASHAs and AWWs lacking access to ORS and zinc at the time of diarrhea consultation are unlikely to advise adequate treatment. As such, diarrhea management training of ASHAs and AWWs should emphasize the importance of referring caregivers to obtain ORS and zinc through other channels if supplies are not directly available. However, more importantly, diarrhea management programs should prioritize ensuring sustainable access to ORS and zinc in order to limit the need for outside referrals.

Among RMPs, there was a strong association between direct access to ORS supplies at the time of the survey and ORS prescribing (Table 5.12). This finding is important because prior to program implementation, RMPs generally did not stock or advise ORS, and the relationship between access and prescribing suggests that increasing the availability of ORS products at RMP practices can help alter RMP prescribing behavior. Still, RMPs commonly advise medications through other channels, such as affiliated local chemists and drug stores, which perhaps explains why direct access to zinc at the time of the survey had no effect on zinc prescribing after controlling for other factors (Table 5.12). Diarrhea management programs should therefore expand private sector program implementation to chemists and drug stores in an effort to promote broad access to ORS and zinc across the private sector.

ASHAs prescribed ORS and zinc with higher odds than AWWs. Although total years of education and the training curricula for ASHAs and AWWs were identical, it is possible that ASHAs were more comfortable in the role of distributing treatment, since they have traditionally carried medical kits and AWWs have only recently begun to fulfill this expectation. Diarrhea management programs operating in the public sector should attempt to build AWWs' capacity and confidence for advising and dispensing treatment.

The internal validity of this study may be limited by the Hawthorne effect, which results when the presence of an outside observer causes an individual to deviate from his or her normal behavior [27]. It is thus possible that the presence of study staff during the observed diarrhea consultation led providers to alter their treatment and prescribing practices. However, due to the overall low frequency of ORS and zinc prescribing compared to reported knowledge during interview, it is unlikely that providers were aware of the observers' research agenda; while providers may have modified their behavior due to the presence of study staff, it is unlikely they adjusted their practices concerning ORS and zinc prescribing—the main study outcomes, thereby reducing the threat to internal validity.

The internal validity of the study's findings on RMPs may also be limited due to selection bias. The random selection of RMPs for inclusion in the study was conducted using a sampling frame comprised of all RMPs that had been identified by FHI360 at the time of the study. However, it is possible that the sampling frame was not representative of the true population of RMPs because the list was generated early in the project and

FHI360 may not have had sufficient time to identify all RMPs located within the district. In addition, a number of RMPs that operate underground to avoid government registration may not have been identified by FHI360 or may not have been located by the evaluation study team during data collection. It is therefore possible that sampled providers are more reflective of registered RMPs than of the actual population of RMPs, and subsequent research findings are potentially less generalizable to those not registered with the government. Still, the threat of selection bias is lessened by the fact that government oversight of informal private sector providers is typically lax in UP, enabling unregistered RMPs to operate more openly. Selection bias would be a more likely threat if the described private sector study design were repeated in a state with stricter enforcement of government regulations concerning informal private sector providers, such as Gujarat, for example.

The external validity of this study is largely dependent upon health system structure and geography, and caution should be taken before generalizing the conclusions of this analysis to regions outside and within India. Conclusions regarding the public sector are likely relevant in states with comparable government sector policies on the role of AWWs and ASHAs as those enforced in Bihar and Gujarat. Similarly, findings concerning RMPs are likely generalizable to states in which the structure of informal private sector providers is akin to that found in UP. Future childhood diarrhea management programs in regions throughout India should glean geographically appropriate evidence for improving ORS and zinc prescribing practices among ASHAs, AWWs and RMPs.

Table 5.1

Probability proportional to size (PPS) sampling in Gujarat and Bihar

District selected by evaluation team	Total number of PHCs in district	Proportion of PHCs in district relative to total # PHCs across selected districts in the state*	Number of PHCs randomly selected in district**
Gujarat			
Patan	36	0.15	5
Surendranagar	43	0.18	6
Banaskantha	85	0.36	12
Sabarkantha	72	0.31	10
Total	**236**		**33**
Bihar			
Banka	11	0.159	6
Bhagalpur	16	0.232	8
Samastipur	20	0.290	10
Sitamarhi	17	0.246	9
Sheohar	5	0.072	2
Total	**69**		**35**

*Calculation: Total # PHCs in district/ Total # PHCs in all districts selected for a given state. At the time of the study, there were 56 PHCs total across the 4 selected districts in UP; 236 PHCs total across the 4 selected districts in Gujarat; 69 PHCs total across the 5 selected districts in Bihar.

**Calculated as the proportion of PHCs in the district relative to the total # of PHCs across selected districts in the state*33

Table 5.2

Sample size calculation for ASHAs and AWWs in Gujarat and Bihar

Assumed proportion prescribing ORS	0.20	0.15	0.10
Allowable margin of error	0.10	0.10	0.10
Required sample size of ASHAs/AWWs*: (A)	165	136	102
Required sample size of ASHAs/AWWs accounting for design effect: (B) = (A)*1.365[1]	226	186	140
Required sample size of ASHAs/AWWs accounting for 15% refusal/missingness : (B)/.85[2]	266	219	**165**

[1]Design effect based on previous study in rural India [28].

[2]Required sample sizes calculated in Stata 12.0 using 80% power and Bonferroni correction for Type I error (i.e. alpha = 0.05/2=0.025) to enable comparisons between AWWs and ASHAs [23].

Table 5.3

Probability proportional to size sampling in UP

District selected by evaluation team	Total # of informal providers in district	Proportion of informal providers relative to total*	Number of Tehsils randomly selected in district**
Ambedkar Nagar	2998	0.07	2
Badaun	3810	0.09	3
Barabanki	3095	0.08	2
Bareilly	5185	0.13	4
Faizabad	3381	0.08	2
Hardoi	4598	0.11	3
Kanpur Dehat	1167	0.03	1
Lucknow	2898	0.07	2
Shahjahanpur	2312	0.06	2
Sitapur	5690	0.14	4
Sultanpur	3662	0.09	3
Unnao	2059	0.05	1
Total	**40,855**	1	**29**

*Calculation: # informal providers in district / # informal providers across all 12 districts (i.e. 40,855)

**Calculated as the proportion of informal providers in the district relative to the total # of informal providers across all selected districts in the state*29

Table 5.4

Sample size calculation for RMPs in UP

Assumed proportion prescribing zinc	0.25	0.2	0.15	0.10	0.05
Allowable margin of error	0.1	0.1	0.1	0.1	0.1
Required sample size*: (A)	157	137	114	86	53
Required sample size accounting for design effect: (B) = (A)*1.365 [1]	215	188	156	118	73
Required sample size accounting for 18.8% missingness: (B)/0.812 [2]	**265**	**232**	**193**	**146**	**90**

[1]Design effect based on previous study in rural India [28].

[2]Required sample size calculated in Stata 12.0 with 5% type I error and 80% power [23]

Table 5.5

Number of providers both observed and interviewed by state and provider type.

State	Provider Type	Number of districts	Providers observed AND interviewed N
UP	RMP	12	97
Bihar	ASHA	5	165
	AWW		165
Gujarat	ASHA	4	165
	AWW		165

Table 5.6

Power to detect the proportion of RMPs, ASHAs and AWWs that prescribed both ORS and zinc to treat diarrhea among children 2-59 months of age*

Private Sector					
Margin of error	**+/- 5%**	**+/- 8%**	**+/- 10%**	**+/- 12%**	**+/- 15%**
Proportion of RMPs prescribing both ORS and Zinc					
0.55	16.89%	35.40%	50.79%	66.19%	84.74%
0.50	16.51%	34.87%	50.40%	66.13%	85.15%
0.45	16.36%	34.93%	50.82%	67.00%	86.35%
0.40	16.45%	35.60%	52.15%	68.92%	88.38%
0.35	16.81%	37.04%	54.60%	72.14%	91.25%
Public Sector					
Margin of error	**+/- 5%**	**+/- 8%**	**+/- 10%**	**+/- 12%**	**+/- 15%**
Proportion of ASHAs and AWWs prescribing both ORS and Zinc					
0.65	47.85%	85.25%	96.18%	99.37%	99.98%
0.60	45.86%	83.82%	95.66%	99.27%	99.98%
0.55	44.70%	83.10%	95.46%	99.25%	99.98%
0.50	44.28%	83.12%	95.62%	99.33%	99.99%
0.45	44.59%	83.90%	96.12%	99.48%	99.99%

*Estimated power calculated in Stata 12.0 at the alpha=0.05 level separately for RMPs (n=97), ASHAs (n=330) and AWWs (n=330) [23].

Table 5.7

Binary variables of zinc and ORS knowledge

Survey question	Binary variables used to construct zinc knowledge index	Binary variables used to construct ORS knowledge index	Binary variables used to construct combined zinc AND ORS knowledge score
Reported treatment for a child with 5 loose/watery stools per day for 3 days and no dehydration	=1 if Zinc = 0 if would not treat child OR did no report zinc OR no response	=1 if ORS = 0 if would not treat child OR did no report ORS OR no response	=1 if zinc AND ORS = 0 if would not treat child OR did no report either zinc or ORS OR no response
Reported treatment for a child with 5 loose/watery stools per day for 3 days, sunken eyes and lethargy	=1 if Zinc = 0 if would not treat child OR did no report zinc OR no response	=1 if ORS = 0 if would not treat child OR did no report ORS OR no response	=1 if zinc AND ORS = 0 if would not treat child OR did no report either zinc or ORS OR no response
Reported treatment for a child with 4 loose/watery stools per day for 15 days	=1 if Zinc = 0 if would not treat child OR did no report zinc OR no response	=1 if ORS = 0 if would not treat child OR did no report ORS OR no response	=1 if zinc AND ORS = 0 if would not treat child OR did no report either zinc or ORS OR no response
Reported treatment for a child with bloody stools	=1 if Zinc = 0 if would not treat child OR did no report zinc OR no response	=1 if ORS = 0 if would not treat child OR did no report ORS OR no response	=1 if zinc AND ORS = 0 if would not treat child OR did no report either zinc or ORS OR no response

Table 5.7 continued

Survey question	Binary variables used to construct zinc knowledge index	Binary variables used to construct ORS knowledge index	Binary variables used to construct combined zinc AND ORS knowledge score
Reported zinc dose for child <6 months	=1 if 10 mg for infants 2-5 months of age =0 if incorrect dose and/or age range specified* OR no response	-	=1 if 10 mg for infants 2-5 months of age =0 if incorrect dose and/or age range specified* OR no response
Reported zinc dose for child 6-59 months	=1 if 20 mg for children 6-59 months of age =0 if incorrect dose and/or age range specified* OR no response	-	=1 if 20 mg for children 6-59 months of age =0 if if incorrect dose and/or age range specified* OR no response
Reported zinc duration	=1 if 10-14 days =0 if incorrect number of days or no response	-	=1 if 10-14 days =0 if incorrect number of days or no response
Reported preparation of ORS for a child 2-59 months of age with diarrhea	-	=1 if 1 L packet in 1 L water OR 200 mL packet in 1 cup water = if incorrect preparation or no response	=1 if 1 L packet in 1 L water OR 200 mL packet in 1 cup water = if incorrect preparation or no response
*Providers were not penalized for slight variations in the interpretation of age cut-offs. The following responses were also considered correct: (1) 10 mg for infants 2-6 months of age; (2) 20 mg for children 6-59 months/ 7-59 months/ 6-60 months/ 7-60 months of age			

Table 5.8

Description of explanatory variables included in multiple logistic regression models

Explanatory variables	Description
Included in public and private sector models	
Child age	0 = 7-59 months; 1= ≤6 months
Child gender	0 = Female; 1 = Male
Training	0 = Did not receive diarrhea management training in the 6 months prior to the survey 1 = Received diarrhea management training in the 6 months prior to the survey
Access to ORS/zinc/both ORS & zinc	0 = Did not have access to ORS/zinc/both ORS & zinc stocks at the time of the survey 1 = Had access to ORS/zinc/both ORS & zinc stocks at the time of the survey
Included in public sector models only	
Provider type	0 = AWW; 1= ASHA
State	0 = Gujarat; 1 = Bihar
ASHA/AWW education	0 = ≤10 years of school; 1 = >10 years of school [a]
Included in private sector models only	
RMP education	0 = ≤14 years of school; 1 = >14 years of school [a]

[a] Threshold of dichotomous variables for education were set at the mean number of years of RMP (13.7 years) and ASHA/AWW (10.2 years) education.

Table 5.9

Reported and observed characteristics of AWWs, ASHAs and RMPs

		AWW [a] (N=330) n (%)	ASHA [a] (N=330) n (%)	RMP [a] (N=97) n (%)
Sex				
	Female	330 (100)	330 (100)	0
	Male	0	0	97 (100)
Age (years): mean (SD)		36.7 (7.6)	31.4 (6.4)	41.1 (11.7)
Religion				
	Hindu	308 (93.3)	315 (95.4)	82 (84.5)
	Muslim	21 (6.4)	15 (4.6)	15 (15.5)
Education (years): median (max, min)		10 (4, 17)	10 (0, 17)	12 (9, 21)
Diarrhea training in the 6 months prior to survey				
	Yes	297 (90.0)	295 (89.4)	67 (69.1)
Access to supplies at the time of survey				
	ORS	145 (43.9)	191 (57.9)	70 (72.2)
	Zinc	272 (82.4)	304 (92.1)	35 (36.1)
	ORS and Zinc	129 (39.1)	182 (55.2)	33 (34.0)
Observed prescribing in consultation with diarrhea case [b]				
	ORS	244 (73.9)	278 (84.2)	55 (56.7)
	Zinc	216 (65.5)	259 (78.5)	27 (28.1)
	ORS and Zinc	216 (65.5)	257 (77.9)	19 (19.6)

[a] AWWs and ASHAs were sampled from Bihar (N=165 AWWs; N=165 ASHAs) and Gujarat (N=165 AWWs; N=165 ASHAs); RMPs were sampled from UP.

[b] Prescribing was defined as having advised a specified treatment regardless of whether the product was directly provided during the consultation or advised through another channel.

Table 5.9 continued

	AWW [a] (N=330) n (%)	**ASHA** [a] (N=330) n (%)	**RMP** [a] (N=97) n (%)
Correct responses to zinc knowledge questions: [c]			
Child with 5 loose/watery stools per day for 3 days and no dehydration	279 (84.5)	291 (88.2)	38 (39.2)
Child with 5 loose/watery stools per day for 3 days, sunken eyes and lethargy	95 (28.8)	109 (33.0)	30 (30.9)
Child with 4 loose/watery stools per day for 15 days and no dehydration	200 (60.6)	212 (64.2)	26 (26.8)
Child with bloody stools	113 (34.2)	140 (42.4)	23 (23.7)
10 mg zinc dose for child 2-5 months of age [d]	115 (34.9)	115 (34.9)	6 (6.2)
20 mg zinc dose for child 6-59 months of age [d]	155 (47.0)	165 (50.0)	6 (6.2)
10-14 days duration of zinc supplementation	278 (84.2)	292 (88.5)	52 (53.6)
Correct responses to ORS knowledge questions: [e]			
Child with 5 loose/watery stools per day for 3 days and no dehydration	320 (97.0)	316 (95.8)	76 (78.4)
Child with 5 loose/watery stools per day for 3 days, sunken eyes and lethargy	110 (33.3)	120 (36.4)	53 (54.6)
Child with 4 loose/watery stools per day for 15 days and no dehydration	223 (67.6)	232 (70.3)	42 (43.3)
Child with bloody stools	123 (37.3)	158 (47.9)	44 (45.4)
ORS preparation: 1 L packet in 1 L water OR 200 mL packet in 1 cup water	309 (93.6)	319 (96.7)	50 (51.6)

Table 5.9 continued

	AWW [a] (N=330) n (%)	**ASHA** [a] (N=330) n (%)	**RMP** [a] (N=97) n (%)
Correct responses to zinc & ORS knowledge questions: [f]			
Child with 5 loose/watery stools per day for 3 days and no dehydration	279 (84.6)	289 (87.6)	35 (36.1)
Child with 5 loose/watery stools per day for 3 days, sunken eyes and lethargy	95 (28.8)	109 (33.0)	28 (28.9)
Child with 4 loose/watery stools per day for 15 days and no dehydration	200 (60.6)	212 (64.2)	25 (25.8)
Child with bloody stools	113 (34.2)	138 (41.8)	15 (15.5)

[a] AWWs and ASHAs were sampled from Bihar (N=165 AWWs; N=165 ASHAs) and Gujarat (N=165 AWWs; N=165 ASHAs); RMPs were sampled from UP.

[b] Prescribing was defined as having advised a specified treatment regardless of whether the product was directly provided during the consultation or advised through another channel.

[c] N (%) responding zinc

[d] Providers not penalized for slight variations in the interpretation of age cut-offs. The following responses were also considered correct: (1) 10 mg for infants 2-6 months of age; (2) 20 mg for children 6-59 months/ 7-59 months/ 6-60 months/ 7-60 months of age

[e] N (%) responding ORS

[f] N (%) responding zinc AND ORS

Table 5.10

Results of principal components analysis (PCA) for public and private sector models

Binary variable	Weights used in construction of zinc knowledge index score	Weights used in construction of ORS knowledge index score	Weights used in construction of combined zinc AND ORS knowledge index score
Public Sector			
Reported treatment for a child with 5 loose/watery stools per day for 3 days and no dehydration	0.67	0.38	0.67
Reported treatment for a child with 5 loose/watery stools per day for 3 days, sunken eyes and lethargy	0.36	0.56	0.35
Reported treatment for a child with 4 loose/watery stools per day for 15 days	0.55	0.71	0.53
Reported treatment for a child with bloody stools	0.40	0.70	0.39
Reported zinc dose for child 2-5 months	0.59	-	0.57
Reported zinc dose for child 6-59 months	0.59	-	0.57
Reported zinc duration	0.71	-	0.71
Reported preparation of ORS for a child 2-59 months of age with diarrhea	-	0.21	0.38

Table 5.10 continued

Binary variable	Weights used in construction of zinc knowledge index score	Weights used in construction of ORS knowledge index score	Weights used in construction of combined zinc AND ORS knowledge index score
Private Sector			
Reported treatment for a child with 5 loose/watery stools per day for 3 days and no dehydration	0.69	0.46	0.63
Reported treatment for a child with 5 loose/watery stools per day for 3 days, sunken eyes and lethargy	0.78	0.76	0.74
Reported treatment for a child with 4 loose/watery stools per day for 15 days	0.68	0.73	0.70
Reported treatment for a child with bloody stools	0.77	0.59	0.72
Reported zinc dose for child 2-5 months	0.11	-	0.24
Reported zinc dose for child 6-59 months	0.07	-	0.21
Reported zinc duration	0.37	-	0.35
Reported preparation of ORS for a child 2-59 months of age with diarrhea	-	0.12	0.14

Table 5.11

Factors associated with prescribing among public sector ASHAs and AWWs

Variable	Adjusted OR [a]	95% CI	P-value
Outcome: Prescribing both ORS and zinc			
ORS and zinc combined knowledge index score	2.48	1.90-3.24	<<0.001
Provider type			
ASHA	1.61	1.05-2.48	0.029
AWW	1.0		
Access to both ORS and zinc at the time of the survey	4.82	1.99-11.71	0.001
Received diarrhea management training in the 6 months prior to the survey	3.96	2.03-7.72	<<0.001
Provider education			
>10 years of school	1.30	0.82-2.08	0.264
≤ 10 years of school	1.0		
Observed child age			
≤ 6 months	0.61	0.37-1.01	0.055
7-59 months	1.0		
Observed child gender			
Male	1.09	0.74-1.58	0.670
Female	1.0		
State			
Bihar	0.56	0.23-1.37	0.202
Gujarat	1.0		

Table 5.11 continued

Variable	Adjusted OR [a]	95% CI	P-value
Outcome: Prescribing ORS			
ORS knowledge index score	1.54	1.24-1.92	<<0.001
Provider type			
ASHA	1.64	1.02-2.66	0.042
AWW	1.0		
Access to ORS at the time of the survey	6.96	2.75-17.61	<<0.001
Received diarrhea management training in the 6 months prior to the survey	4.00	2.16-7.38	<<0.001
Provider education			
>10 years of school	1.15	0.70-1.91	0.578
≤ 10 years of school	1.0		
Observed child age			
≤ 6 months	0.66	0.40-1.10	0.109
7-59 months	1.0		
Observed child gender			
Male	1.18	0.78-1.78	0.445
Female	1.0		
State			
Bihar	0.58	0.24-1.40	0.225
Gujarat	1.0		

Table 5.11 continued

Variable	Adjusted OR [a]	95% CI	P-value
Outcome: Prescribing zinc			
Zinc knowledge index score	2.14	1.70-2.70	<<0.001
Provider type			
ASHA	1.74	1.10-2.75	0.018
AWW	1.0		
Access to zinc at the time of the survey	17.42	6.59-46.06	<<0.001
Received diarrhea management training in the 6 months prior to the survey	3.07	1.64-5.76	<<0.001
Provider education			
>10 years of school	1.26	0.79-2.00	0.336
≤ 10 years of school	1.0		
Observed child age			
≤ 6 months	0.52	0.31-0.89	0.016
7-59 months	1.0		
Observed child gender			
Male	1.09	0.74-1.61	0.665
Female	1.0		
State			
Bihar	3.14	1.56-6.34	0.001
Gujarat	1.0		

[a] Estimates were calculated using logistic regression with the robust cluster estimator of variance in Stata 12.0 [23].

Table 5.12

Factors associated with prescribing among private sector RMPs

Variable	Adjusted OR [a]	95% CI	P-value
Outcome: Prescribing both ORS and zinc			
ORS and zinc combined knowledge index score	2.32	1.29-4.17	0.005
Access to both ORS and zinc at the time of the survey	1.42	0.37-5.51	0.613
Received diarrhea management training in the 6 months prior to the survey	0.88	0.24-3.25	0.844
Provider education			
>14 years of school	3.31	0.96-11.38	0.057
≤ 14 years of school	1.0		
Observed child age			
≤ 6 months	3.82	0.39-37.18	0.248
7-59 months	1.0		
Observed child gender			
Male	1.90	0.40-8.97	0.420
Female	1.0		

Table 5.12 continued

Variable	Adjusted OR [a]	95% CI	P-value
Outcome: Prescribing ORS			
ORS knowledge index score	1.28	0.79-2.07	0.318
Access to ORS at the time of the survey	8.56	2.81-26.11	<<0.001
Received diarrhea management training in the 6 months prior to the survey	0.96	0.33-2.76	0.942
Provider education			
>14 years of school	0.62	0.21-1.82	0.384
≤ 14 years of school	1.0		
Observed child age			
≤ 6 months	2.06	0.21-20.33	0.537
7-59 months	1.0		
Observed child gender			
Male	1.37	0.51-3.67	0.528
Female	1.0		

Table 5.12 continued

Variable	Adjusted OR [a]	95% CI	P-value
Outcome: Prescribing zinc			
Zinc knowledge index score	3.57	2.08-6.13	<<0.001
Access to zinc at the time of the survey	0.60	0.16-2.26	0.452
Received diarrhea management training in the 6 months prior to the survey	1.61	0.45-5.71	0.464
Provider education			
>14 years of school	4.24	1.34-13.40	0.014
≤ 14 years of school	1.0		
Observed child age			
≤ 6 months	2.02	0.30-13.47	0.466
7-59 months	1.0		
Observed child gender			
Male	1.44	0.36-5.71	0.606
Female	1.0		

[a] Estimates were calculated using logistic regression with the robust cluster estimator of variance in Stata 12.0 [23].

Figure 5.1

Boxplots showing ORS, zinc and combined ORS and zinc knowledge index scores for public sector ASHAs and AWWs

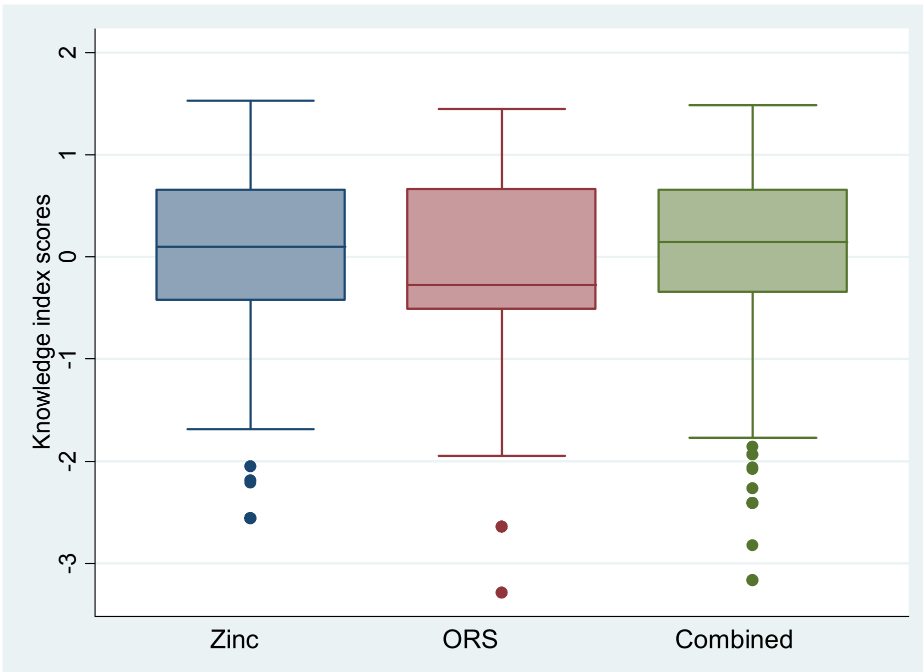
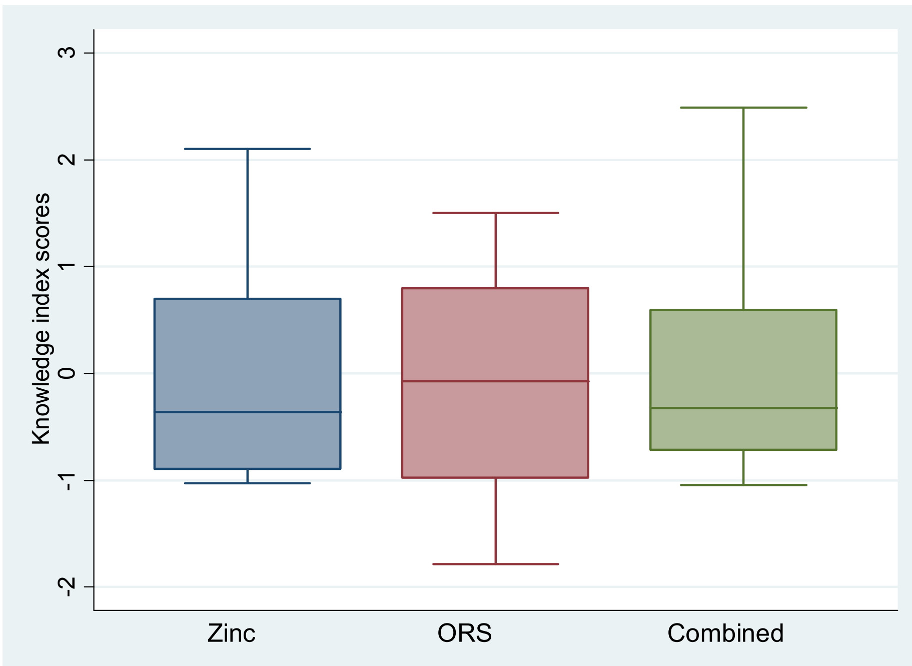


Figure 5.2

Boxplots showing ORS, zinc and combined ORS and zinc knowledge index scores for private sector RMPs



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Chapter Six: Conclusions and Recommendations

6.1 Summary of Major Findings

The findings of this dissertation have highlighted factors of potential importance to programmatic activities and evaluations centered on reducing the burden of diarrhea among children under-five. Using data from the large-scale evaluation of a program implemented in three states in India, this dissertation assessed the household- and village-level influences of diarrheal illness, care-seeking and treatment (Paper 1); the role of episode severity on caregiver recall, care-seeking and treatment (Paper 2); and the association between provider knowledge and observed ORS and zinc prescribing practices (Paper 3). The results of Papers 1-3 are connected thematically and together comprise evidence that may prove useful in future efforts to scale-up oral rehydration salts (ORS) and zinc for the treatment of diarrhea among children under-five in regions generalizable to Uttar Pradesh (UP), Gujarat and Bihar, India.

The results of Papers 1 and 2 illustrate the important role of caregiver education on care-seeking for diarrheal episodes among children 2-59 months of age. Caregiver education beyond primary school (>7 years) was strongly associated with seeking care outside the home in two distinct models, which indicated a significant effect size after controlling for either village variation (Paper 1) or episode severity (Paper 2). Furthermore, Paper 1 established a trend and Paper 2 identified an effect of caregiver education beyond primary school on increased odds of ORS use. These findings suggest that programs should focus efforts to promote care-seeking and ORS/zinc treatment on households with less educated caregivers.

Similarly, the results of Paper 1 show the importance of caregiver education in conferring protection against diarrheal infection; however, this effect was not evident among caregivers from households with no access to a toilet or latrine. The interaction between household sanitation practices and caregiver education signifies that increased education alone may not substantially reduce the risk of diarrhea if exposure to diarrheal pathogens persists in the household environment. At the village-level, increases in the aggregated proportion of caregivers educated beyond primary school were protective against diarrheal infection—an effect which is likely mediated by village-level improvements in sanitation. These findings shed light on the need for evaluations to consider population-level education and sanitation when assessing programmatic impact, since unaccounted discrepancies in these variables across comparison groups or over time could lead to biased conclusions.

The results of Paper 2 highlighted the inherent bias of cross-sectional data collection with two-week recall. Episodes with more distant onset compared to the survey date were underrepresented in the data; whereas, reported symptoms of fever, vomiting, increased maximum stool frequency, and dehydration were associated with more distant as opposed to more recent recall among caregivers. These findings indicate that the household coverage surveys underestimated overall two-week prevalence whilst overestimating the proportion of episodes of perceivably higher severity. Since recall error for the period 1-7 days prior to the survey was drastically reduced compared to the period 8-14 days beforehand, the accuracy of evaluation data would be improved by cross-sectional data collection with one-week recall. Although decreasing the recall interval results in increased sample size requirements that may not be logistically feasible, evaluation surveys designed with two-week recall should also include questions on one-week recall, so that key outcomes for coverage of care-seeking and ORS/zinc can be estimated for both intervals and compared.

Both Papers 1 and 2 underscore the association between state of residence and care-seeking. The odds of seeking care outside the home through any channel were higher in UP compared to Gujarat (Papers 1 and 2) and Bihar (Paper 2); however, the odds of seeking care through the public sector alone or through both the public and private sectors were lowest in UP (Paper 2). Among those that sought care, the odds of ORS (Papers 1 and 2) and zinc (Paper 2) use were elevated if care was sought through the public sector, but this effect was modified by state with only a trend established for UP and larger effect sizes for both Bihar and Gujarat. In addition, the effect of public sector care-seeking on zinc use was larger for Bihar than Gujarat (Paper 2), and this result was mirrored by Paper 3 in which Accredited Social Health Activists (ASHAs) and Anganwadi workers (AWWs) advised zinc with higher odds in Bihar compared to Gujarat. These findings point to inter-state differences in care-seeking and prescribing practices that may affect program outcomes and impact. Programmatic and evaluation activities should account for inter-state differences by setting state-specific benchmarks for outcomes and impact.

Paper 3 illustrated the link between provider knowledge and prescribing practices, highlighting the importance of educating ASHAs, AWWs and informal private sector rural medical practitioners (RMPs) in adequate management of diarrhea among children under-five. Paper 3 also established the need for periodic reinforcement of training among ASHAs and AWWs, since higher odds of advising ORS and/or zinc were associated with receipt of training in the 6 months prior to the survey. On the other hand, training had no effect on the prescribing practices of RMPs, which indicates the need to reevaluate whether visits by pharmaceutical representatives are the only mechanism by which informal private sector providers can be educated on adequate diarrhea treatment for children under-five.

Finally, the results of Paper 3 also emphasized the extreme importance of ensuring sustained access to ORS and zinc supplies in the public sector. ASHAs and AWWs without access to ORS/zinc at the time of the observation did not commonly advise ORS and zinc through another channel. As such, diarrhea management programs should provide adequate support to the ORS/zinc supply chain. In addition, trainings should include instruction on the channels through which to advise ORS/zinc in the event of stock-outs.

6.2 Recommendations for Future Research

Future research should be conducted to expand upon the findings of this dissertation. Paper 1 was limited by the dearth of village-level data on sanitation, economic development, and the availability of health infrastructure. It is likely that variation at the village-level was not adequately captured by the sole use of aggregated household-level variables. The multilevel analyses should therefore be conducted again for all outcomes in order to assess whether inference is affected by the inclusion of additional village-level predictors. Ideally, follow-up analyses would include data on village sanitation, water sources and proximity to public and formal private health sector channels, such as Primary Health Centers (PHCs), district hospitals and private hospitals.

The inclusion of data on the number of schools located within villages and distance from major roadways would also improve the models.

The findings of Paper 2 would be furthered by additional research on local terminology for diarrheal episodes in young children in UP, Gujarat and Bihar. Follow-up studies should aim to identify and define terms, as well as assess their influence on recall, care-seeking and treatment. Subsequent studies should also evaluate why care is sought for certain episode symptoms and not others in order to increase understanding of local perceptions of severity of diarrheal illness among children under-five.

Moreover, follow-up studies to Paper 2 should utilize evaluation data to determine whether programs with limited resources can maximize their impact by promoting care-seeking and ORS/zinc treatment for all diarrheal episodes or solely those of perceivable severity. In the latter case, additional research is warranted to identify the specific severity criteria for which caregivers should be told to seek care and ORS/zinc treatment, and these criteria should be translated into promotional messages and communications materials.

In light of the findings of Paper 3, future research should address how to improve the training of informal private sector RMPs. It is unlikely that the group meetings used to train ASHAs and AWWs would be sufficient for RMPs, since they typically operate independently. However, studies should assess whether the quality of one-on-one RMP training could be improved by covering different topic matter or by increasing the duration and/or frequency of visits. Additional follow-up studies on RMPs should assess what motivates their prescribing behavior and whether zinc prescribing is equitable, since RMPs stand to profit from its sale.

Furthermore, subsequent studies should evaluate whether caregivers of children advised to obtain ORS/zinc through alternate channels actually do so. Addressing this research question would bring to light the true implications of failing government sector supply chains, since ASHAs and AWWs without product have no alternative than to refer caregivers to other channels for treatment. A follow-up study should assess the proportion of referred caregivers that follow through on such referrals and the proportion that ultimately obtain ORS/zinc, since these figures are of importance to coverage estimates.

The association between the recommendations of providers and the actions of caregivers should also be evaluated through a study on zinc adherence. While zinc is advised for 10-14 days, it is possible that caregivers fail to administer the full dose since diarrheal episodes are typically short in duration. Evaluations may find that in the event of low adherence to zinc, high zinc coverage does not necessarily translate to high zinc impact.

Finally, it is possible that some of the findings of this dissertation are not externally valid given the diverse health infrastructure across Indian states. The research questions addressed by this dissertation should therefore be repeated using evaluation data from countries and states in India and that are not generalizable to UP, Bihar and Gujarat.

Curriculum Vitae

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EDUCATION

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May 2008	**Master of Health Sciences (MHS)** Department of International Health, Program in Global Disease Epidemiology and Control, Johns Hopkins Bloomberg School of Public Health Baltimore, MD Advisor: Dr. Christian Coles Practicum: "Analysis of the 2007 Peruvian Maternal and Child Health Delivery Channel Survey (MCHDCS)"
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2012- 2013	Health Information Technology for Economic and Clinical Health, Office of the National Coordinator (ONC) Funding Award
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PROFESSIONAL TRAINING

2012- 2013	Public Health Informatics Certificate Program Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

PROFESSIONAL EXPERIENCE

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Research Associate, Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Coordinates research activities and conducts statistical data analyses for a large-scale evaluation of a program aimed at reducing the burden of diarrheal morbidity and mortality among children under-five in Uttar Pradesh, Gujarat and Bihar, India.

May 2008-Aug 2009

Monitoring & Evaluation Coordinator, Department of Global Programs, CMMB, New York, NY

Conducted field visits to Kenya and India to oversee monitoring and evaluation activities and trainings for HIV/AIDS and child health programs. Designed data collection instruments, protocols and databases. Performed statistical analyses of monitoring and evaluation data.

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Data Analyst, Unit of Family and Child Health/Child and Adolescent Health, Pan American Health Organization (PAHO), Washington DC

Conducted statistical data analysis of the Maternal and Child Health Delivery Channel Survey (Peru 2007). Prepared analytical protocols and guidelines for use by in-country data analysts.

May 2007-Sep 2007
Health Research Training Program Intern, Bureau of Communicable Disease, NYC Department of Health and Mental Hygiene, New York, NY
Performed statistical data analyses to assess the burden of imported dengue cases in NYC.

May 2005-Sep 2006
Research Assistant, Robert Wood Johnson Health and Society Scholars Program, Columbia University Mailman School of Public Health, New York, NY
Managed databases and aided in statistical analyses for social and environmental epidemiology projects.

CONSULTATIONS

Feb 2013-May 2013
Bureau of Epidemiology Services, Program Collaboration and Service Integration (PCSI), NYC Department of Health and Mental Hygiene, New York, NY
Developed stored SAS processes to generate tables and conduct real-time analyses in order to integrate infectious disease data from TB and HIV/AIDS programs into DOHMH online EpiQuery system.

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Performed data analyses to estimate global morbidity and mortality due to *Shigellae* and ETEC.

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- American Public Health Association, Jan 2010-Present
- IUNS International Congress of Nutrition, Sep 2013
- GETHealth Summit, Feb 2013
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- Columbia Undergraduate Public Health Society, Cofounder, Sep 2003-May 2006

EDITORIAL ACTIVITIES

Paediatric and Perinatal Epidemiology

TEACHING EXPERIENCE

2010-2012 Teaching Assistant, Department of International Health,
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- *Clinical and Epidemiologic Aspects of Tropical Diseases*
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Peer-reviewed articles

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Book chapters

Fischer-Walker CL, **Lamberti L**, Roth D, Black RE. "Zinc and Infectious Diseases." Zinc in Human Health. Ed. Lothar Rink. Amsterdam: IOS Press, 2011. 234-53.

SCIENTIFIC PRESENTATIONS

Lamberti LM, Fischer Walker CL, Taneja S, Mazumder S, Black RE. "Zinc and ORS for the treatment of childhood diarrhea in India: the association between provider knowledge and practice." *IUNS International Congress of Nutrition.* Granada, Spain. Sep. 2013.

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SCIENTIFIC MEETING ABSTRACTS

Fischer Walker CL, Perin J, Aryee M, **Lamberti L**, Black RE. "Diarrhea incidence and severity among children under 5 years of age in low and middle-income countries" *ASTMH Annual Meeting*. Philadelphia, PA. Dec 2011.